Gynecological Pathology

A Manual of Microscopic Technique and Diagnosis in Gynecological Practice For Students and Physicians

BY

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TRANSLATED AND EDITED BY

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With a Chapter on the Embryology of the Female Genitalia and the Pathological Growths Developing from Embryonal Structures

ILLUSTRATED BY ONE HUNDRED ENGRAVINGS

NEW YORK

WILLIAM WOOD & COMPANY

MDCCCCI

PRESS OF STETTINER BROS.,
22-26 DUANE ST., N. Y.

TO

GEH. MED.-RATH PROF. DR. WALDEYER

MY HIGHLY ESTEEMED TEACHER

THIS BOOK IS DEDICATED WITH FEELINGS OF

GRATITUDE AND ADMIRATION

CARL ABEL

PREFACE TO THE SECOND EDITION.

Since the appearance of the valuable investigations of Ruge and Veit, the microscopical examination of tissue excised and curetted from the uterus has become a necessary adjunct to gynecological diagnosis, so far as such diagnosis is concerned with affections of the uterus. The necessity of this method of diagnosis has been called to the attention of physicians by the numerous works on this subject. It is therefore natural that a much larger percentage, not only of specialists, but also of general practitioners, should seek knowledge of this subject. The numerous individual works scattered in various journals and archives make its study a question of time and patience. These works, which follow one or another of the numerous questions into minute details, are in nowise calculated to interest a beginner. In the large text books this branch of gynecology has received attention, but much that is important is dismissed with a few words. To overcome these difficulties is the purpose of this book, which is intended to serve as an introduction to practical experience.

Due weight is given to the consideration of normal conditions, for a knowledge of these is necessary before one can appreciate pathological changes. This is especially true of the uterus, since its structure is normally subject to many variations.

References to the literature are made only where necessary. The drawings, which with few exceptions are taken from my specimens, have been taken directly from the true microscopical picture, and schematic drawings have been avoided, since the latter are not suitable for practical instruction.

The second edition has been considerably enlarged, especially the chapters on the vulva, vagina, tubes, and ovaries. Although not treated generally *in extenso*, I have given what my experience has proved to be absolutely necessary and of PRACTICAL GYNECOLOGICAL VALUE.

CARL ABEL.

BERLIN, July, 1899.

PREFACE TO THE TRANSLATION.

In spite of the glowing results obtained in operations for carcinoma of the cervix and uterus, so far as immediate mortality goes, only a small percentage fail to suffer from a recurrence of this malignant growth. In no branch of medicine, therefore, is an EARLY DIAGNOSIS so necessary. Since the great majority of patients see their physician before consulting a gynecologist, the onus of making a correct diagnosis rests with him, and it is his duty to make a test excision from the cervix, or a test curettage of the uterus in all cases where the possibility of the presence of a malignant growth is suspected. Aside from this the various forms of endometritis, polypus, sarcoma, etc., can be diagnosed only by microscopical examination, and early malignant changes can be recognized. Then again the differential diagnosis between abortion and extrauterine gestation is all-important and may frequently be made by microscopical examination of expelled particles. The value of a microscopical diagnosis is also evident in the case of tuberculosis or gonorrhea of the genitalia. Having been associated for a long period with Dr. Abel in his pathological work, I realize that this book meets most fully the demands not only of the specialist, but also of the beginner, for it is the result of clinical experience and is intended for practical purposes only. In translating this book, I feel that a most valuable addition is made to our at present meagre diagnostic repertory, and that the adoption of methods here described will be the means of saving many a life. The chapter on embryology and on the origin of growths from embryonal cells and organs has been added by me as an aid to the understanding of what is, perhaps, the most interesting part of pathology. In no other portion of the body are these processes more complex and in no other area is the theory of Cohnheim so well exemplified.

SAMUEL WYLLIS BANDLER.

NEW YORK, November, 1901.

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PART I.

TECHNIQUE.

I. MATERIAL.

WITH the development of the bimanual method of examination in gynecology, diagnosis has reached such a state of perfection that by this means alone certain affections of the uterus or its adnexa may be determined with certainty. In a certain class of cases—those in which there are changes in the inner surface and in the vaginal portion of the uterus—the sense of touch alone does not suffice to make an exact diagnosis. The examining finger is, with justice, called "the eye of the gynecologist," yet on palpation we are often liable to illusions, and for that reason the sense of sight cannot be dispensed with. The introduction of the vaginal speculum enables us to view directly the lower part of the uterus; yet this method also fails, because no definite conclusions as to the anatomical structure of an affected organ can be made from its macroscopical appearance alone. This, added to the fact that the inner surface of the uterus is not accessible to the eye, makes it necessary, in doubtful cases, to remove pieces from the cervix and from the lining of the uterus, by test excision and by test curettement, for microscopical examination. In this manner we are able, by viewing the pathological specimens, to verify a previous clinical diagnosis. That even then an absolute, positive statement cannot be made will be shown more clearly later on. Nevertheless, the importance of such an examination is evident; for upon its result will always depend the objective and scientific basis for therapeutic action.

The affections of the external genitalia and of the vagina lead to a microscopical examination only in rare cases. This method is chiefly made use of in pathological conditions of the portio vaginalis, the cervix, and the endometrium.

Harpooning large abdominal tumors is now entirely discontinued, since exploratory laparotomies have been generally accepted. Likewise the microscopical examination of fluid obtained by puncture leads to a positive result only in those cases in which specific form elements are found, viz., echinococcus hooklets, etc. Otherwise more knowledge is gained by chemical examination, if a preliminary observation be needed to form a diagnosis.

1. OBTAINING THE MATERIAL.

Before removing a portion of the uterus a precise history of each case should be obtained, and a bimanual examination then determines whether an affection of the cervix or of the body of the uterus is present. It is necessary from the beginning to know whether a test excision from the cervix or a test curettement of the cavity of the uterus is required.

In carrying out this slight procedure it is necessary to expose the organ as far as possible. If done with assistance, it is better to use the Sims-Simon anterior and posterior specula. The anterior lip of the cervix is grasped by means of a bullet forceps or a uterine clamp and is carefully drawn down, and firmly fixed after removing the anterior speculum.

It may be mentioned that care is needed in the procedure, so that too much tension should not be exerted if the adnexa of the uterus are

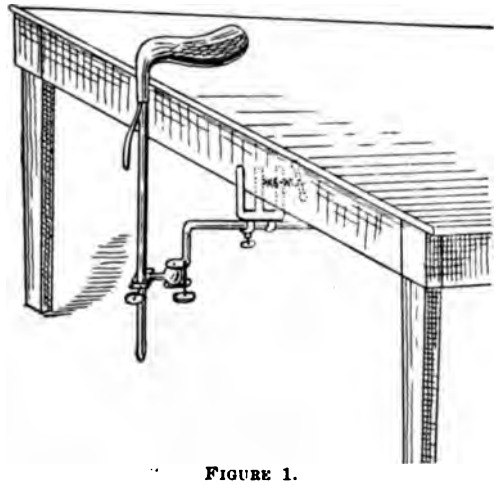

FIGURE 1.

not quite free; for then a parametritis or an inflammatory condition of the tubes is present, and careless or violent traction upon the uterus may easily cause great harm. The presence of such a condition should be, to the beginner, a contraindication.

If no assistance is at hand, a self-supporting speculum may be used to advantage. There are many such specula; any one is good which accomplishes the chief requisite—viz., no interference with the instruments used or with freedom of movement. For this purpose I use, as a rule, a speculum modified by L. Landau and myself, which has the special advantage that it may be attached not only to the examining table but also to any table or bed. It is therefore suited to the use of the general practitioner. It consists of a binding screw with spaces for a horizontal arm (Fig. 1) which ends in a ball-and-socket joint. The latter is intended to hold the rather

long rod on which the usual Simon speculum is fitted. The joint, if tightened, permits of fixing the speculum in any desired position and follows as far as may be needed the movement of the hand. When the speculum has been placed in the necessary position and fastened there by a screw, both hands are free to introduce the anterior speculum, to grasp the uterus, and to carry out further manipulations without special difficulty. The self-retaining speculum of Neugebauer, junior, may be especially recommended, as well as the speculum of Edebohls (Fig. 1*a*).

(A) TEST EXCISION FROM THE CERVIX.

No especial preparations are needed in making a test excision from the *portio vaginalis*. After introduction of the speculum, the vagina

FIGURE 1*a*.—EDEBOHLS' SPECULUM.

and external surface of the cervix should be thoroughly cleansed with a three per cent solution of carbolic acid or with a 1:5000 bichloride solution. It is best to first irrigate the parts and then energetically wash them with cotton dipped in this solution.

After fixing the anterior lip of the cervix with the forceps, a wedge-shaped piece is cut from the desired area with Cooper's or any other angular scissors. Care should be taken to remove not only the affected portion, but, if possible, to select an area which shows the transition from healthy to diseased tissue. The resulting bleeding can usually be arrested by packing with cotton, yet at times one or two ligatures may be needed. At any rate, it should be made a general rule that the patient lie quietly for some time after, to convince one's self that the bleeding has entirely ceased, for in some cases, even after such a slight

procedure, severe bleedings may result unless sufficient precaution has been taken.

(B) Test Curettage of the Endometrium.

After disinfection of the vagina and traction upon the cervix, the length and course of the uterine canal must be determined with the sound, and the permeability of the internal os, as well as any perceptible changes in the mucous membrane, must be recognized.

I consider it absolutely inadvisable to probe the uterus blindly without introducing the speculum, since it is impossible to be certain that this is performed with perfect asepsis. This naturally holds good also for the curettage and for every instrumental intrauterine procedure.

Under control of the eye we enter the uterine cavity with a middle-sized curette and remove the mucous membrane by energetic movements from above downward. The small particles thus obtained are caught in a clean glass held in front of the speculum. In most cases this comparatively simple method suffices. If, however, the amount of mucous membrane obtained is insufficient for microscopical examination, or if it be thought that the affected areas have not been obtained, it is advisable to dilate the cervix and then penetrate to the fundus with the finger. In this way the pathological region may be felt with greater certainty and a portion removed with the finger or scraped away with a sharp spoon. If the uterus be once dilated so that the examining finger easily enters it, there is no danger in energetically scraping with a spoon. It is certain that with this instrument more material may be obtained than with the curette.

By what means the dilatation of the cervix shall be accomplished is a matter for the individual operator to decide. Some prefer rapid, others gradual dilatation. The former can be easily done with the Fritsch dilators; the latter is best attained by the introduction of iodoform gauze into the uterine cavity. I always use the latter method according to the suggestion of L. Landau. With a metal introducer a strip of gauze five metres long is pushed up to the fundus and the uterine cavity packed as tightly as possible. The remainder of the strip fills out the cervix and is held by a cotton tampon placed in front of the cervix. The gauze is left for twenty-four hours, when in most cases the examining finger may be introduced without difficulty. If, however, this be impossible, it is necessary to renew this packing only once to obtain the desired result, even in the case of the virgin uterus. This procedure should, if possible, not be an ambulatory one.

(C) Test Excision from the Vagina and External Genitalia.

In the case of doubtful macroscopical affections of the vagina or external genitalia a portion of the diseased tissue may be removed, under

aseptic precautions, with scissors or the knife; the bleeding is stopped by suture or by a dressing.

II. FURTHER TREATMENT OF THE MATERIAL OBTAINED.

The excised pieces, or the particles curetted from the uterus, are cleaned under slowly running water and are then viewed with the naked eye or through a magnifying glass. A close examination of the specimen in this fresh, so-called "living" condition should never be neglected; for its color, consistence, and character must be observed. At times it is of advantage to make a sketch and an exact record, since subsequent manipulations essentially change the appearance of the specimen. Therefore it is advisable, at the same time, to decide what method of hardening will be adopted for its microscopical examination, and in what direction the sections are later to be made.

The method of preparing the material depends essentially on the quantity at our disposal. Contrary to general pathological examinations, where, as a rule, larger portions of the various organs are used, we usually in these cases have to do with small bits. Therefore, although the examination in a fresh condition is to be desired, we are often unable to do so; for we must consider that the examination of fresh specimens often furnishes no positive means of diagnosis, as only the examination of numerous sections shows us the true nature of the affection. To examine the living specimen it is necessary to divide it, so that eventually the other half may be embedded. As a rule, however, the material is not sufficient to permit of such a course, especially that obtained by a test curettage.

On the other hand, a dangerous operation often depends on the microscopical diagnosis made from relatively very small bits of tissue. Therefore it is necessary to use all the finer means placed at our disposal through modern microscopical technique in making such a diagnosis positive. For that reason I advise that an excised portion of the cervix be so divided that one part may be examined in its fresh state and that the other be put in absolute alcohol or in another fixing fluid (page 8) and prepared for finer sections. Curetted particles, on the contrary, may be best put immediately into absolute alcohol and the examination of fresh specimens may be dispensed with. This should be the case only when large quantities are not at our disposal, for such an examination discloses much to us which cannot be seen in hardened sections.

1. EXAMINATION OF FRESH SPECIMENS.

The fresh specimen should be put at once in the so-called "physiological salt solution" (0.75 per cent), in which the individual elements are perfectly preserved in their original form. They may then be ex-

amined as teased specimens or in sections cut by the freezing microtome. The latter method is most suited to our purpose, as the relation of the various structures to one another is not changed, and it permits of a correct judgment of the condition before us. By teasing the specimens we isolate the several elements from each other, and it is impossible to decide whether the surface epithelium sends processes into the tissue or whether we are concerned with a simple hyperplastic or a destructive process—points of decisive value in making a diagnosis.

Formerly fine sections were made with scissors or razor. These methods are of no value in the case of such material as is at our disposal, because the fixing of the specimen in liver or in some other sub-

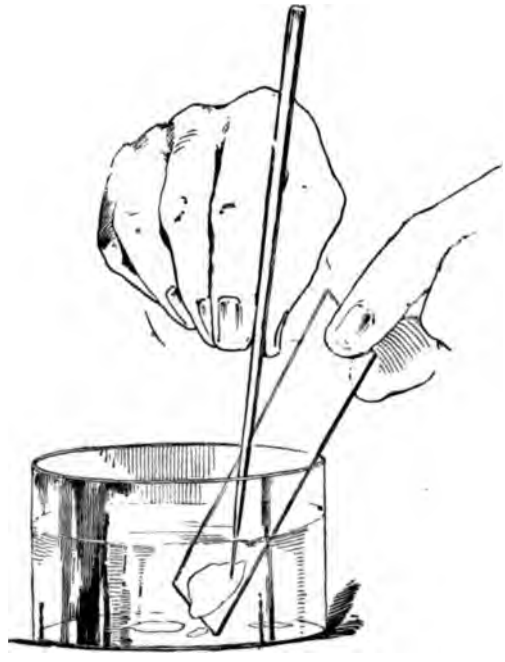

FIGURE 2.—TRANSFERRING THE SECTION TO THE SLIDE WITH A GLASS NEEDLE. *(After O. Israel.)*

stance destroys the tender epithelium upon the surface as well as the glandular formations.

Therefore it is best to cut the fresh specimen with the freezing microtome, but not into too fine pieces; very thin pieces usually tear during subsequent manipulation. Each section must be removed from the blade of the knife with a fine camel's-hair brush and placed in a bowl of distilled water, thereby avoiding the air bubbles which rise to the surface on thawing of the sections, and which often adhere to them if ordinary salt solution or glycerin be used. To prevent tearing of the sections on transmission to the slide, it is better to push the slide under the section as it swims in the fluid, holding it gently with a glass rod (Fig. 2).

After spreading the section carefully upon the slide it is covered with a fine cover-glass. The latter should be grasped at one edge with a pincers, and the other side should be brought at an acute angle upon the fluid covering the surface of the slide, and gradually released. The superfluous fluid is removed with blotting paper. The fresh section is then ready for examination and may be studied in its unchanged form with a high or low power. When dealing with unstained sections the slide should be placed upon a dark under-layer. This simple procedure greatly aids the manipulation of unstained sections.

The examination of such specimens has various and often important advantages over the examination of specimens changed by hardening. Only in fresh cuts do we see the cells as they were during life, and the amount of fat, as well as any existing degenerations, may be determined.

In addition, various micro-chemical reactions may be viewed—a step which should not be undervalued, for it sometimes gives us important information. To make a section more transparent, we may add under the edge of the cover-glass a drop of diluted acetic acid (two to three per cent). A bit of blotting paper put on the other side of the cover-glass causes the acetic acid to penetrate the specimen quickly. In this way rather thick sections may be so cleared up that a positive diagnosis may be made. Alcohol and chloroform or ether may be put under the cover-glass, if it is desired to remove the fat elements.

To prove the presence of elastic fibres, caustic soda in a one to three per cent solution may be used. In this way a marked swelling of the albuminates, of the lime-producing substances, and of the contractile elements of the smooth and striated muscles and of the nuclei is produced; also horny substance becomes quite transparent. An especially valuable result is obtained by a thirty-three per cent solution of caustic potash. In this most of the elements are preserved, while the cement substance is dissolved. If a piece of a uterine myoma be put for a few minutes in this solution, it separates under the needle, almost of itself, into the individual cell fibres. Red blood cells preserve their form well in this solution (Friedländer).

Bleedings into tissues or a plethora of the blood vessels can in no way be so well observed as in fresh specimens. These may be permanently preserved if the water or common salt solution be replaced by glycerin or by a fifty-five per cent solution of potassium acetate. The latter is preferable, because in glycerin the sections become so clear that after a time many points can no longer be observed; at the same time the cells after long-continued action of the glycerin change their form.

The method recommended by Pick is the best for obtaining permanent specimens of frozen sections. It consists in the use of alum-carmin combined with formalin; to the well-known alum-carmin of Grenach (containing four to five per cent of carmin) is added Schering's forma-

lin, 10 to 100, which solution may be preserved in a dark bottle. The method of Pick is as follows:

1. Preparation of the frozen section with Jung's microtome.
2. Transfer of the section into four per cent formalin solution, ¼ minute.
3. Formalin alum-carmin, 2 to 3 minutes.
4. Washing in water, ½ minute.
5. Alcohol, eighty per cent, ½ minute.
6. Absolute alcohol, 10 seconds.
7. Carbol-xylol, ½ minute.
8. Canada balsam.

Often on examining these sections we find ourselves compelled to make larger sections, and series of sections with differentiating stains. Then this simple method is no longer sufficient and the specimen must be made more resisting; it must be hardened and embedded in a firm substance which may at the same time be cut by the microtome knife.

2. FIXING THE SPECIMENS.

Fixing the tissue elements is desirable for further minute examination. For this purpose, besides alcohol, the so-called "fixing fluids" may be used, of which I mention the following:

(a) Müller's solution (see below).

(b) Saturated watery solution of corrosive sublimate.

(c) Zenker's fluid (Müller's fluid 100.0 plus bichloride 5.0. Shortly before using add 5.0 glacial acetic acid).

Fixing with the bichloride requires two hours if the pieces be not too large; with Zenker's fluid, twenty-four hours. Before the pieces, after being fixed, are put into alcohol, they must be washed thoroughly in running water for at least twenty-four hours.

(d) Flemming's solution (acetic acid 25.0; chromic acid, 3.75; osmic acid, 2.0; distilled water to 500).

Specimens cleansed of blood are put for four to six hours in this solution; are then soaked and preserved in alcohol (sections to be stained with safranin).

3. HARDENING AND EMBEDDING THE SPECIMENS.

With our methods of examination it is of the utmost importance to obtain a diagnostic result as quickly and surely as possible, the anatomical questions connected therewith being of secondary importance. The specimen is therefore put into absolute alcohol at once as mentioned above. The use at first of dilute alcohol and then of stronger and stronger solutions I consider, at least for our purposes, to be unnecessary. For preparing small pieces I use a glass cylinder six to

eight centimetres high and three to five centimetres wide, with flat bottom and cork stopper. These may also be used in the further steps of preparation; the labelling of every glass should never be neglected. If the alcohol be removed two or three times within twenty-four hours, the specimen has then the necessary consistence for cutting. The simplest process would be to cut the piece between hardened amyloid liver, but this is inadvisable since the surface epithelium is easily destroyed. It is of the greatest importance in our examinations to compress and damage the tissues as little as possible. It is therefore most rational to stick the specimen upon a cork or piece of wood, which may be fastened in the clamp of a microtome. The specimen itself is thus protected from injury. For this purpose we use:

(A) Glycerin-gelatin for Fastening the Specimen.

After the specimen has lain for several hours in absolute alcohol it is pasted to the cork of the glass cylinder with glycerin-gelatin. The cylinder is filled with fresh absolute alcohol, and is left with the cork downward until the next day (Fig. 3, *b*).

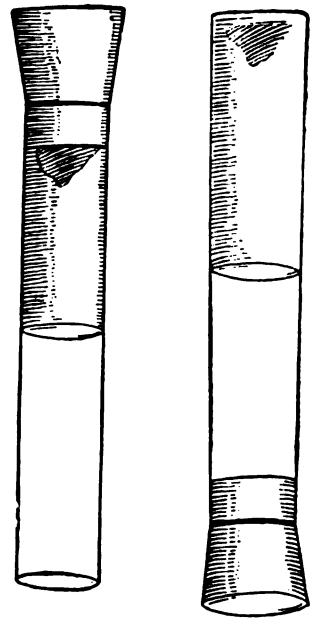

Figure 3.

a, glass cylinder for preserving the specimen to be examined; *b*, the same used for hardening the specimen fastened to the cork.

The specimen has then the necessary firmness for cutting with a microtome; the alcohol may be renewed several times if desired, though this step is not necessary.

The cork is then fastened in the microtome clamp so that the specimen is not injured. The glycerin layer surrounding it prevents the direct contact of the knife upon its surface during the cutting. In this way a tender epithelium covering the surface is usually retained *in toto*.

The preparation of the gelatin is simple. Ten grammes of the finest gelatin is put into a well-cleaned vessel and covered with water. After four to six hours the gelatin is sufficiently swollen, and, after pouring off the water, may be easily liquefied by moderate heating. While stirring with a glass rod ten grammes of glycerin and five drops of carbolic acid are added; this mixture is left in a wide-necked vessel.

To paste a specimen upon a cork a piece of this gelatin is taken and made fluid by heating. A thin layer is poured upon the surface of the cork, and the previously hardened specimen placed upon it and covered on all sides with fluid gelatin. If it is desired that no part of the upper layers be lost, the whole specimen may be covered with a mantle of gelatin, which becomes firm after a short time. The specimen is ready for cutting the next day if immersed in absolute alcohol. This proceeding has the advantage that good sections may be obtained with rapidity, and may subsequently be stained by any desirable method.

(B) Cutting Alcohol Specimens with the Freezing Microtome.

Recently the following method has been recommended: After hardening small pieces for several hours in absolute alcohol, they are put for two hours in a four per cent solution of formalin, then placed in water for half an hour, after which they may be cut with a freezing microtome. Even pieces which have lain for longer periods in alcohol may, if put in two per cent formalin for two to six hours (according to their size), be cut with a freezing microtome. This method, introduced by Benda, has the advantage that, although the alcohol is removed, the fixing of the tissue is not affected. It is, however, impossible to make a large series of sections of specimens prepared in this manner, and it is frequently necessary to make a series of sections not only for finer anatomical examination but also to insure a positive diagnosis. We will discuss those methods which make this possible.

We are concerned here with the so-called "embedding" of the specimens, *i. e.*, their saturation with a substance at first fluid, but later solidifying, which adapts itself to every fold and cavity, and preserves their form when solidified. The most convenient and satisfactory method for our purpose is:

(C) The Embedding of Specimens in Celloidin.

The fresh specimen is put for twelve to twenty-four hours in absolute alcohol (according to its size) and for the same length of time in sulphuric ether.

When freed from water by this means it is put into a thin liquid solution of celloidin. Celloidin is cut into small pieces and dissolved in equal parts of absolute alcohol and ether. A thin or thick solution may be obtained, depending upon the amount of alcohol and ether used. The specimen while in thin celloidin should be entirely covered by it, remaining for twenty-four hours in an air-tight bottle. At the expiration of this period the specimen is placed in a thick solution of celloidin, a small slit being left in the covering of the vessel so that the alcohol and ether may evaporate very slowly. After a few hours the celloidin becomes cloudy and of semi-solid consistence. It is then possible to cut out the specimen with its mantle of celloidin and to paste it with thick celloidin upon cork or wood, after which it remains for twelve hours in seventy to eighty per cent alcohol, when it has obtained the proper consistence for cutting. This method, with the above-mentioned advantages, takes four to five days. A more troublesome method, but one which at times must be used, is:

(D) The Embedding of Specimens in Paraffin.

This method is used for our purposes only in making serial sections. It is better to stain such specimens *in toto,* but pieces too large to insure proper staining should not be taken. Pieces one centimetre wide and two centimetres thick are best; pieces more than four centimetres thick should never be used, if possible. The fresh specimen is put into dilute alcohol, which must be renewed at times until it remains perfectly clear; it is then placed in the staining solution. Very good results are obtained with Böhmer's hematoxylin; eosin and safranin are also suitable. The specimen, according to its thickness, remains two to eight days in the well-filtered solution. An over-staining is not to be feared; even if the external part be darkly tinged this is better than having the central portions unstained by too rapid methods. From the staining solution the specimen is put into seventy per cent alcohol, where it lies for twenty-four hours, being then dehydrated in absolute alcohol. It is then put for twelve hours in xylol to prepare it for saturation with paraffin.

The saturation with paraffin is accomplished as follows: A mixture of xylol and paraffin, equal parts, is made by melting paraffin of a low melting point over the flame and adding an equal quantity of xylol. In this the specimen remains for twenty-four hours at a uniform temperature of 37° Centigrade, in a paraffin oven with thermostat, and is then put into pure paraffin at a constant temperature of 48° to 50° Centigrade. The paraffin is then permitted to solidify at room temperature, and the paraffin block, containing the specimen and cut down to proper size, is fastened with paraffin upon a cork or wood and is then ready for cutting. Such blocks may be preserved in a dry condition as long as is desired. If these directions are followed closely a complete

series of sections may be cut. The individual sections are thinner than those obtained by any other method. Of course, as in all technical processes, practice is required, but patience should not be lost if first attempts fail.

The methods with which the specimens prepared in these different ways should be cut with a microtome will be discussed in the next chapter.

4. CUTTING HARDENED OR EMBEDDED SPECIMENS WITH A MICROTOME.

In cutting, the microtome knife is so placed that its entire cutting edge may be used. It must therefore form a most acute angle with the specimen. The blade of the knife and the specimen itself must be constantly moistened; only frozen and paraffin specimens are cut dry with the knife in a transverse position. The body which holds the knife must be moved evenly and not too quickly; the runners must be well oiled. The thickness of each section should always be alike; sections of fifteen to twenty microns are as a rule sufficient for our purpose. One should not believe that the thinnest sections always reveal the most. Only those specimens hardened in alcohol and embedded in gelatin or those held between bits of liver should be moistened with absolute alcohol; those embedded in celloidin should be moistened with seventy to eighty per cent alcohol.

As numerous sections one after another are generally made, a small bowl filled with dilute or absolute alcohol should be placed on a dark under-layer next to the microtome, and the sections should be transferred from the blade to the solution with a fine camel's-hair brush. The cuts are naturally much shrivelled by the alcohol and should be placed in water for several minutes before staining. They then spread out, lose their folds, and regain very nearly their original form. They are then transferred to the staining fluid by means of a spatula.

A very different technique is required for cutting specimens embedded in paraffin. These sections are generally quite thin and cannot, as in other methods, be transferred from one vessel to another, therefore all the manipulations must be accomplished on the glass slide. I, as a rule, make use of the following method: In a wide-necked bottle absolute alcohol is poured over collodion, covering it entirely. Of this solution, which keeps well if corked thoroughly, one drop is placed upon the slide, and the section, transferred from the knife with a soft brush, is pressed down upon it firmly with filter paper. In this way the section is firmly fixed and the superfluous fluid is at the same time removed. In the same manner the second and the following sections are placed in a row, the sign of an arrow being made upon the slide to show in which direction the series runs. To give the whole a pleasing appearance a piece of white paper with uniform fields marked upon it is put

under the glass slide, and the sections are attached to the slide at equal distances from each other.

When a glass slide is covered with ten to twenty sections, according to the size of the specimen, the paraffin is dissolved by pouring xylol over the whole slide, making each cut transparent. The superfluous xylol is removed by pouring it into a small bowl (this xylol can be used several times). The sections are then covered with xylol and Canada balsam, equal parts.[1] When putting on the cover-glass care should be taken to avoid air bubbles, which are often annoying. One should not be sparing with the Canada balsam, for whatever runs over may be easily removed. The cover-glass should be held at one side with a forceps and should be lowered slowly upon the balsam. The large cover-glasses which are used should be well cut; it is necessary to observe that they are not too thick, for if they are it is difficult to use powerful magnification.

We have here discussed purposely only the cutting of hardened specimens with a microtome; for, with the small amount of material generally at our disposal, sections made with a razor, even if skilfully done, give us little aid and waste our scanty material. In addition the sections are thicker than those made with a microtome, and errors in judging the microscopical picture are easily made—viz., an epithelial growth in glands may be diagnosed when in reality it is simply an illusion due to the thickness of the sections. At any rate, serial sections can never be made with the hand.

5. STAINING THE SECTIONS.

It is not our purpose to consider here all the methods of staining which have been used since the introduction of this procedure. For our purpose good results are obtained with very simple stains. I use exclusively hematoxylin or picrolithiocarmin (Orth), but examine every section, and this is decidedly to be recommended, first unstained, in water or glycerin.

(A) PICROLITHIOCARMIN.

This exceedingly good contrasting stain, introduced by Orth, is prepared as follows:

Solution I.: A cold saturated solution of lithium carbonate, in which carmin powder dissolves in any desirable amount—2.5 grammes of powder to 100 grammes of lithium carbonate solution is a combination which may be recommended; lithiocarmin.

Solution II: Saturated solution of picric acid.

One part of Solution I. to two parts of Solution II. gives a good picrolithiocarmin solution.

[1] If the sections are not previously stained, this may be done on the slide, all the sections being stained at one time. Xylol, absolute alcohol, 96 per cent alcohol, water, stain, water, alcohol, xylol, Canada balsam.

This stain is best used for only those specimens hardened in alcohol. Those specimens prepared in glycerin-gelatin stain a deep red.

The section, after it has been spread out in water, should be placed in this stain with a spatula for five to ten minutes, when it is then deeply stained. A special advantage of this stain is that even if the section remains in it for a longer period it is not over-stained. The section is then put for one to two minutes in alcohol containing hydrochloric acid (one part hydrochloric acid to one hundred parts of seventy per cent alcohol), and is then washed in dilute alcohol and dehydrated in absolute alcohol. The specimen is then made clearer in oil of cloves, oil of bergamot, or in xylol, and then transferred by a spatula to the slide and spread out so that no folds are present. After removing the superfluous oil it is mounted in Canada balsam. The latter may be kept of a proper consistence by the aid of chloroform or xylol.

By this method the nuclei become a deep red while the protoplasm is scarcely stained. Horny cells, as well as fibrin, hyaline substances, and red blood corpuscles, take on a yellow color. The nuclei of squamous epithelium become a pale pink, fibrillar connective tissue remains undyed, so that the whole makes a clear picture of the specimen thus stained.

The specimens embedded in celloidin do not give as good results by this method as with hematoxylin, which I prefer for that reason.

(B) HEMATOXYLIN.

To prepare this stain, if not desirous of using the purchasable Delafield's hematoxylin, use the following method: One gramme of hematoxylin is dissolved in 30 grammes of absolute alcohol. A solution of powdered alum is prepared, 0.5 to 1 gramme of alum in 30 cubic centimetres of distilled water. Into this is shaken drop by drop the alcoholic solution of hematoxylin until the fluid takes on a deep violet color. It is then left for several days in an uncovered wide-necked vessel, when it becomes darker. Before using it must be carefully filtered.

It should be a general rule to filter all staining solutions before use. For this purpose I have used for years bottles with glass funnels. The filter paper lining the funnel serves to close the bottle, so that the solution is quite protected from impurities.

Sections embedded in celloidin remain longer than the ordinary alcohol sections in this solution (ten to twenty minutes or more, according to size and thickness), and are then placed for a short time in alcohol containing hydrochloric acid until they begin to assume a red tint, and are then placed in seventy per cent alcohol. It is well to leave the sections then in absolute alcohol until the mantle of celloidin begins to curl. Care must be taken that the alcohol does not dissolve all the celloidin, for then very fine sections easily fall to pieces. The section is then made transparent in oil of bergamot or in xylol. If at

this stage the celloidin mantle becomes milky or cloudy, the specimen must be put again into absolute alcohol until the cloudiness has disappeared.

The section is then put with a spatula upon the slide and mounted in xylol-Canada balsam, after removing the oil with filter paper.

The advantage of this method is the splendid staining of the nuclei. The protoplasm is faintly stained, the celloidin not at all. If it be desired to stain the protoplasm also, eosin[1] may be used later, which, with hematoxylin, gives very clear pictures. Such a double method is not absolutely necessary for our diagnostic purposes. When one has gained sufficient technique with both of the above-mentioned methods other procedures will scarcely be needed.

(c) Staining of Elastic Fibres.

Recently the staining of elastic fibres has been brought into prominence (Meissner). Since this is of importance in the case of the female genitalia, and especially in the case of malignant tumors, these methods will be mentioned:

1. Taenzer's Orcein Stain.

The sections are taken from water and put for six to twelve hours or longer in orcein solution (Grübler's orcein 0.5, alcohol 40.0, aq. dest. 20.0, acid. hydrochlor. gtt. xx.), and are then placed for a few seconds in hydrochloric acid alcohol (acid muriatic 0.1, ninety-five per cent alcohol 20.0, aq. dest. 5.0), where they become differentiated, and are then, after they have taken on a wine-red color, washed in water. Then dehydration in absolute alcohol five to ten minutes. They are then cleared in oil and mounted in Canada balsam.

The elastic fibres appear an intense red upon a pale pink background.

2. Weigert's Fuchsin-Resorcin Stain.

Staining solution.—Of a resorcin-fuchsin mixture (resorcin 2.0, fuchsin 1.0, distilled water ad 100.0) 200 c.c. are put into a porcelain bowl and brought to boiling; then 25 c.c. ferri liq. sesquichlor. (German Pharmacopeia) are added and the whole is allowed to boil, with stirring, two to five minutes more. A muddy deposit is formed. The mass is allowed to cool (it need not get quite cold) and is then filtered. What runs through the filter is thrown away; the deposit is left upon the filter until all the water has dripped off. The filter is then taken off the funnel and put with the deposit in a bowl, in which it is boiled, under constant stirring, with 200 c.c. of ninety-four per cent alcohol. During the boiling the filter paper is removed. The solution is

[1] A concentrated alcoholic solution of eosin is put drop by drop into 96 per cent or absolute alcohol till the latter assumes a rose-red color. In this mixture the specimen is left from a few minutes to several hours. In a watery mixture of eosin of like strength specimens remain only a few minutes.

then permitted to cool and is filtered, and the filtrate is, by the addition of further alcohol, brought to 200 c.c. After adding 4 c.c. of hydrochloric acid the solution is ready for use.

Staining.—In this solution the sections are placed for twenty minutes to one hour, washed in alcohol and cleared in XYLOL *(not in oil of cloves). Carbol-xylol* and *aniline oil with xylol* cannot be used.

After staining, the elastic fibres appear dark blue, almost black, on a quite light background. The nuclei may be stained then with any good carmin. Washing in HCl-alcohol does no harm.

The unstained sections may be preserved in one of the above-illustrated glass cylinders in absolute or dilute alcohol, depending upon their hardening in alcohol or their embedding in celloidin; for it is often necessary after some time to again examine a specimen for one reason or another.

6. STAINING OF MICRO-ORGANISMS.

Of the micro-organisms found in the female genital canal, the gonococcus and the tubercle bacillus are of special practical importance for our diagnostic purposes. These are sought for either in the secretion or in sections. In the former case, glass slide or cover-glass specimens of the secretion are made by spreading it on and letting it dry. These specimens are first allowed to dry in the air, and are then carefully drawn several times through a flame. They are then ready for staining, and there is no fear that during the subsequent manipulations the secretion will be washed off.

(A) THE GONOCOCCUS.

(*a*) *Dry Cover-Glass Specimens.*

In general the following simple proceeding suffices:

1. Covering the dry specimen with a watery concentrated methyl blue solution (Unna).
2. Heating till it steams.
3. Washing in water.
4. Drying with filter paper.
5. Embedding in Canada balsam.

In this way the gonococci as well as the other cocci are stained a deep blue. The gonococci are characterized by the fact that, lying in pairs next to each other ("biscuit-shaped"), they appear mostly in small groups inside the protoplasm of the pus cells. Sometimes they lie outside of the cells and may then be mistaken for other cocci, if it were not possible to use a method of differentiation. This method we possess in the shape of Gram's decolorizing method with Lugol's solution, by which the gonococci are decolorized while the other pathogenic and non-pathogenic cocci retain their stains. By subsequently or previously

staining with a contrasting color the gonococci are then differently stained.

Gram's Method.

The dry cover-glass or slide specimen is stained with picrocarmin or with thin fuchsin solution, washed in water, and dried. It is then stained for one-half minute with Ehrlich's aniline water-gentian violet solution, and then (without washing) for one minute with Lugol's solution (1 iodine, 2 potassium iodide, 300 water), and then moved in alcohol until maximum decolorization is obtained. The specimen is washed in running water, dried, and mounted in xylol-Canada balsam (Günther). The gonococci are found to be red, while the other cocci are stained blue.

(*b*) *Cut Sections.*

To find the gonococci in sections is much more difficult than in dry specimens. Practice is necessary to obtain good stains. The method of Wertheim is as follows:

1. Sections are put in aniline water-gentian violet 3 to 5 minutes (not longer, for then the celloidin is affected).
2. Lugol's solution, about 1 minute.
3. Ninety-five per cent alcohol for decolorizing (this should not be complete; the section must still have a distinctly violet color).
4. Watery methyl blue solution, for a few minutes.
5. Absolute alcohol, ½ to 1 minute.
6. Oil of bergamot.
7. Canada balsam.

The most essential and difficult point is to observe the proper limit when removing the methyl blue by alcohol. If this process be too short, then the gonococci are not distinctly seen on the too dark background; if too long, then the gonococci are also decolorized.

(B) TUBERCLE BACILLI.

The staining is best managed by means of

(*a*) *Gabbet's Quick-Staining Method.*

1. Dry specimen is stained ten minutes in carbol-fuchsin (fuchsin 1.0; alcohol 10.0; acid. carbol. 5.0; aq. dest. 100.0).
2. Washing in water.
3. Drying with filter paper.
4. Sulphuric acid-methyl blue solution (methyl blue 2.0; acid. sulph. 25.0; aq. dest. 100.0) five minutes.
5. Washing in water.
6. Drying with filter paper. If red areas are still present the specimen must be put again for several minutes in the sulphuric acid-methyl

blue solution. After drying, the specimen must have a light blue appearance.

7. Canada balsam.

The tubercle bacilli are then red; everything else is stained blue.

(*b*) *Sections.*

For staining sections we use either warm carbol-fuchsin solution (the section is put into the staining fluid, which has been heated and removed from the flame), or the section is put into the cold solution for twenty-four hours. After treatment with sulphuric acid-methyl blue solution the section is dehydrated in alcohol, cleared in xylol, and mounted in Canada balsam.

III. THE MANAGEMENT OF MATERIAL OBTAINED BY LAPAROTOMY OR AUTOPSY.

The specimen, concerning which in its fresh state all necessary notes as to size, color, and consistence are made, must be cleansed under running water of gross impurities and is then put in

1. Seventy per cent Alcohol.

This is renewed regularly until it remains perfectly clear. Care should be taken that the fluid is always a few centimetres above the specimen, as it otherwise easily dries up.

Alcohol is without doubt the most convenient and best preserving material for specimens which must later be examined microscopically. At times we are forced to use

2. *Müller's Fluid,*

when, for instance, it is necessary to examine placentæ and we desire to preserve the blood corpuscles in an unchanged condition.

Müller's fluid is composed of

Potassium bichromate	2.0
Sodium sulphate	1.0
Distilled water	100.0

How long the specimen should remain in this fluid depends upon its size; an entire uterus, for instance, requires about eight weeks. After twenty-four hours the fluid, as a rule, becomes cloudy and should be renewed. If the specimen is completely saturated it is then kept in eighty per cent alcohol, after having been first washed under running water for several hours. If it is desired to fix other form elements (division of nuclei, etc.), small dice-shaped pieces must be cut out of the specimen and put into suitable fixing fluids (see above).

In recent years, for fixing and preserving specimens, great importance has been attached to

3. *Formalin.*

Commercial formalin is a forty per cent solution of formaldehyde. As a rule a four per cent aqueous solution of formalin is used. In this the specimens remain for twenty-four hours and are then put, after thorough washing, into alcohol of increasing concentration. Formalin is at the same time a fixing and a hardening fluid, and has, in addition, the power of preserving the natural color of the specimen. Therefore in place of alcohol the specimens may be preserved in a two per cent solution of formalin.

In preparing the specimen for microscopical examination everything depends upon its character. Definite rules cannot be made. The specimen should be preserved macroscopically as far as possible. Large sections which give a general idea of relations are of special value for judging many anatomical processes. For instance, it is not difficult to make sections through the entire length of the uterus. With practice these may be made so thin that they may be examined with a high-power lens. Good results in such cases depend upon careful embedding and upon a large, sharp knife which does not feather. For embedding such large specimens, which, however, should not be more than 1 cm. in thickness, celloidin gives the best results.

The specimen, well hardened in absolute alcohol, is put for several days in sulphuric ether and then for three to six days in very thin celloidin in an airtight jar. It is then placed for two to three days in thick celloidin, likewise under an airtight cover, which at the expiration of this time is opened a very little so that the ether evaporates slowly. When the celloidin solidifies, the specimen, with its mantle of celloidin, is fastened upon a suitable block and is put into seventy per cent alcohol. In twenty-four hours the specimen is ready for cutting.

While cutting the large specimen it must be constantly moistened by a flow of seventy per cent alcohol. For this purpose a special supply apparatus is used (see appendix). The blade of the knife must also be constantly moistened. Even in these large sections the knife must be drawn through evenly and not too quickly, and the section must be smoothed out with a brush. Sections of twenty to thirty microns are quite suitable.

In further manipulations large glasses like watch glasses are used. The individual steps in the process of staining, washing, and clearing are the same as already described, but demand, on account of the size of the specimen, much more time. It is advisable, if sufficient material is at hand, to make sections vertical as well as parallel to the surface, for just such sections often give information not to be obtained in any other way.

IV. APPENDIX TO PART I.

INSTRUMENTARIUM.

1. Needle holder. The best are those in which the needles may be changed. Wooden handles are better than bone.

2. Spatula, of various sizes, with very thin, supple blades.

3. Brushes, as soft as possible and of various sizes.

4. Scissors, large and small, straight and bent like Cooper's scissors.

5. Forceps—those made by Katsch, in Munich, are very good, and are recommended by Waldeyer for practice in preparing specimens. In Berlin they may be procured of Thamm and Schmidt.

6. Knife (razor) hollowed out on one side only. A double knife is unnecessary.

7. Microtome. The choice of a microtome is not easy, as on its quality depends the character of the sections. If a large model can be obtained this is advisable, for this suffices for all sections, even the smallest. The smaller instruments, on the contrary, do not suffice for the larger sections.

A freezing apparatus is very desirable for our purposes. Jung in Heidelberg and Schwarze in Leipzig furnish this apparatus suited to a microtome. It is advisable, however, to procure a special freezing microtome for preparing frozen sections. Such a microtome is no dearer than the other accessory apparatus and possesses many advantages. For this latter purpose the lever microtome of Jung is to be recommended. The short knives are better able to stand the wear and tear than the large ones of the other apparatus, which are intended to cut only embedded specimens.

For general work I have used for years the large model of Jung. A smaller one is sufficient for diagnostic purposes only, and the difference in cost is so small that it is better to select at once the larger model, for after a short acquaintance with the smaller size one finds the larger quite necessary.

In the instrument of Jung the specimen is lifted by forward movement on an oblique plane. The microtome screw is excellently made, the knife carrier is stable, the clamp holding the specimen may be fixed in any position, the knife is perfect, so that with this instrument perfect sections, from the smallest to the largest size, can be made. The knife carrier is moved either with the hand or with the lever. I prefer to use the hand. For the large specimens special blocks with grooved surfaces should be obtained and made to fit in the specimen clamp. The smallest specimens are fastened to cork and then grasped by the clamp. In cutting, the specimens must be moistened with alcohol by a brush; for the larger specimens an apparatus with a constant flow of alcohol is indispensable. Of knives, two small and two large ones must be selected.

They should be carefully dried with a soft cloth and stropped before using, but not too often and only on a soft leather surface.

The runners on which the knife carrier rests must be oiled with bone-oil, so that only slight force is necessary to make it pass along the entire length of the instrument. After use the microtome should be carefully cleansed of oil and alcohol.

8. An apparatus which gives a constant supply of alcohol, drop by drop.

9. A small paraffin oven with thermostat.

10. Glass vessels of various sizes, cylinders for the specimens, etc.

PART II.

DIAGNOSIS.

To form an opinion of pathological changes it is necessary to have an exact knowledge of normal conditions. This is the more important since the female sexual organs, even under normal conditions, are subject to changes in their anatomical character. For instance, what is normal in a woman who has passed the climacterium may be pathological in a patient in the prime of life. In the same way conditions during and after pregnancy, before and after menstruation, must be viewed from a different standpoint in the case of the uterus of a nullipara or primipara and in that of a multipara. In the following description of normal conditions it must be clearly understood what is meant by the word "normal." As is customary, we accept as normal types those anatomical states in which the organs are found between two menstrual periods. The different variations from the normal which must be considered in diagnosis will be discussed wherever necessary.

I. VULVA.

1. NORMAL ANATOMY.

Under vulva we understand the labia majora, the labia minora, the clitoris, the glands of Bartholini, and the corpus cavernosum of the urethra.

The labia majora are puffy prominences of the skin, which under normal conditions meet in the median line. Their microscopical structure corresponds exactly to that of the external skin. Under many layers of squamous epithelium, which cover the subcutaneous tissue and the papillæ, lie sebaceous and sweat glands, hair, etc. The underlying connective tissue is loose and wavy; between its bundles lie blood vessels and wide lymph spaces; in the deeper layers an abundance of fat tissue is present.

The surface of the labia minora (nymphæ), which are covered by the labia majora, has the character of the skin in general and shows sebaceous glands, but has the appearance of a mucous membrane, since it is moistened by the secretion of the vagina and of the glands of Bartholini. The anatomical structure is the same; yet hair is missing here. At the

vaginal inlet, in the virgo intacta, a semicircular wall is formed by the hymen, so that in this way a boundary is placed between the external and internal genitalia.

The hymen is a crescent-shaped membrane. It is covered on its inner and outer surfaces by stratified, squamous epithelium, beneath which lies connective tissue rich in nuclei. In the papillæ of the hymen are nerve end bulbs, just as in the external skin.

Just in front of the hymen, in the so-called vestibule, open two large mucous glands, the so-called glands of Bartholini.

2. PATHOLOGICAL ANATOMY.

(A) Inflammations.

The inflammations of the vulva affect chiefly the smaller labia and the vestibule, and are most frequently *gonorrheal.* Such inflammations are usually attended by a profuse purulent secretion. In this secretion gonococci are usually found. The smaller lips are then very red and edematous. Frequently small superficial excoriations are present and bleed easily. The microscopical picture shows the subepithelial tissue to be very vascular and to contain solid groups of round cells. These penetrate the epithelium, loosen it, and thus prepare it for shedding. The gonococci also penetrate the epithelial layer and may be found in sections of the underlying tissue.

Secondary inflammations of the vulva occur especially in septic affections in childbed.

(B) Ulcerations.

The most important and most frequent ulcerations are *syphilitic.* These are not to be distinguished microscopically from simple ulcers. The edge of these usually round ulcers is hard. In connection with such ulcers the labia majora may become edematous and firm. Much less frequent are the *tubercular* ulcers (lupus vulvæ). These are to be diagnosed microscopically through the presence of tubercles containing giant cells. It is rarely possible to find tubercle bacilli in them.

(C) Atrophy.

In addition to the atrophy of the external genitalia occurring normally in advanced age through disappearance of adipose tissue, there is observed, in some instances, a peculiar atrophic condition which is called KRAUROSIS VULVÆ.

As a result of the thorough microscopical investigations of Orthmann and Peter in the clinic of Martin, this process must be considered a chronic inflammatory hyperplasia of the connective tissue with a tendency to cicatricial contraction, inflammatory edema of the superficial layers of the corium and the epidermis, and degeneration of the elastic

tissue. This condition is often connected with so-called pruritus vulvæ, which shows itself clinically as an unbearable itching. In the latter no anatomical changes may be found; it may be that it is an affection of the nerve ends which is as yet not recognized. The pathological changes connected therewith are to be considered as secondary and caused by scratching. These changes include a small-celled infiltration of the upper layers under the squamous epithelium, which is in spots hypertrophic.

(D) HYPERTROPHY.

Hypertrophies involve either the epithelium or the connective tissue. The former occur by far the more frequently.

(a) Epithelial Hypertrophies, Pointed Condylomata (CONDYLOMATA ACUMINATA).

The pointed condylomata are growths of the squamous epithelium and the papillæ, which rise above the surface in a wart-like manner, and which, on account of the many depressions between the elevations, give the growth a cauliflower appearance. As a rule, these condylomata are small, the size of a pea or a bean. Through coalescence of a large number of such formations large tumors of the vulva may result. Because of their uneven surface they may be easily taken for carcinomata. Here the microscopical examination is decisive, for it is seen that these epithelial growths are confined solely to the surface; they are simply elevations and thickenings of epithelium which do not grow into the deeper tissues and destroy them. In long-standing condylomata the surface may become ulcerated, and is then covered with a greasy, purulent layer, which makes a confusion with carcinoma still easier. The underlying connective tissue is found in an inflammatory state, showing small-celled infiltration and numerous new formations and ramifications of the papillæ.

Most frequently these pointed condylomata develop in connection with a gonorrheal vulvitis. It must be positively understood that other inflammatory or chronic irritations may also cause the formation of condylomata. Such epithelial growths may develop especially as a result of irritations present during pregnancy. During this time unusually large tumors may be formed.

Whether condylomata are of gonorrheal origin or not can be determined only by showing the presence of gonococci. A small quantity of the secretion is spread upon a glass slide with a previously heated platinum needle, and, after being dried in the air, should be stained with a watery solution of methylene blue. For this purpose I have found the polychrome methylene blue of Unna very serviceable. A few minutes suffice for the staining; the slide is then washed with water and dried with filter paper, and can be examined in oil immersion even without a

cover glass. The gonococci show the well-known biscuit form through the apposition of cocci in pairs, and lie generally in the cell protoplasm. As a rule several nuclei are found in the pus cells.

If a positive diagnosis is to be made and confusion of the gonococci with other cocci is to be avoided, the specimen should be decolorized in the manner described above, according to the method of Gram. In this way the gonococci lose their stain while the other cocci retain theirs. It is then only necessary to employ a contrast stain, viz., Bismarck brown, to be enabled to see the gonococci colored brown in contrast to the other cocci stained blue (see page 17).

(*b*) *Connective-Tissue Hypertrophy.*

In this category must be considered ELEPHANTIASIS VULVÆ. This occurs unilaterally or bilaterally and forms large nodulated tumors of semi-solid consistence. Microscopically there is found a considerable increase of the connective-tissue stroma, with numerous dilated lymph vessels filled with lymph cells. An increase of the elastic tissue likewise takes place. Some authors describe an hypertrophy of the epithelium. In a case observed by me and thoroughly examined, the microscope showed the epithelium to be astonishingly thin—a condition caused, no doubt, by the great stretching and growth of the underlying tissue, with which the growth of the surface epithelium did not keep pace.

(E) NEOPLASMS.

Epithelial growths and growths of the connective-tissue tissues may be distinguished. The former are observed more frequently than the latter. Both, however, are rare.

(*a*) *Epithelial Neoplasms.*

(*α*) Carcinoma.

Carcinomata of the vulva always originate from the squamous epithelium of the surface. Groups of epithelial-like cells force their way into the deeper structures and destroy the tissues originally present. The carcinomata correspond in structure to the typical carcinomata of the skin. Therefore we find here, in the carcinoma nests, central hornification, the so-called carcinomatous pearls. In one case operated upon by me carcinomatous thrombi were found at a very large number of points in the blood vessels, whereby rapid propagation was naturally aided. This extension occurs not only through the blood vessels, but especially through the lymph channels. One finds, therefore, relatively early metastases in the inguinal glands. These also show the structure of squamous epithelium carcinoma.

Most of these carcinomata begin at the outer surface of the vulva. In rare cases primary carcinomata of the clitoris occur.

(β) Cysts of the Vulva.

The cysts occurring on the large and small labia are retention cysts of the sebaceous glands. Furthermore cysts of the glands of Bartholini, especially of their excretory canal, occur. These result chiefly in connection with an inflammatory process and possess, in case of simple inflammation, thin fluid contents. If, however, the cause of infection is gonorrheal, there results an obstruction in the excretory duct and an abscess is formed. In the pus removed from these cysts gonococci are usually found.

Finally, cysts of the hymen have been described. These are lined either with squamous or ciliated or simple cylindrical epithelium. What the origin of these cysts may be has not been established with absolute certainty (see Part III.).

(*b*) *Neoplasms of the Connective Tissues.*

Of these only *fibromata* may be mentioned, for they are the most frequent and may reach a very great size. Furthermore, in individual but very rare cases myomata, lipomata, myxomata, etc., have been observed. All these tumors of the vulva resemble in their structure the same tumor forms occurring in other parts of the body, and offer no difficulties in the way of diagnosis. Sarcomata are found here rarely, mostly as mixed tumors, such as fibro- and myxosarcomata, and more frequently melanosarcomata.

II. VAGINA.

1. NORMAL ANATOMY.

The vaginal mucous membrane does not line this canal with an even surface, but forms numerous elevations and depressions (rugæ and columnæ rugarum).

The surface epithelium is a stratified squamous epithelium, into which the papillæ of the underlying tissue project. The stroma is connective tissue containing few cells, in which no glands are present. In the deeper layers are muscle fibres and fat tissue. Some authors describe glands, lined with cylindrical or ciliated epithelium, as normal constituents of the mucous membrane. According to recent and harmonious opinions it must be concluded that such a condition is rather pathological. I have never found glands in the normal mucous membrane of the vagina. Occasionally in the deep grooves of the lining membrane cylindrical or ciliated epithelium may be found instead of squamous epithelium. Such conditions are doubtless the result of embryonal disturbances, for originally the entire genital tract is covered or lined with cylindrical epithelium (see Part III.).

2. PATHOLOGICAL ANATOMY.

(A) INFLAMMATIONS.

Practically, the most important is the inflammation which occurs in gonorrhea, and which causes the mucous membrane to be covered with small nodules—granular vaginitis. Microscopically this condition shows a marked infiltration of lymphoid cells, limited entirely to the superficial layers. These cells penetrate the epithelium and cause it to be loosened and thrown off. At the height of these nodular elevations the epithelium is very thin and may be easily lifted off. Then erosions result. In the secretion desquamated epithelial cells and pus cells with gonococci are found.

A different but rare form of inflammation is CYSTIC VAGINAL HYPERPLASIA, also called emphysema of the vagina or KOLPITIS EMPHYSEMATOSA. In this condition cysts are formed which lie close under the surface, and are filled with gas. This consists partly of air, partly of trimethylamin. The mucous membrane is very red. Microscopically a decided small-celled infiltration of the stroma is found. This affection is observed during pregnancy; as to its cause nothing positive is yet known.

(B) ULCERATIONS.

Ulcerations in the vagina are either of a *traumatic* nature (pressure of a ring or other foreign body, bedsores, or rather decubitus ulcers, in prolapse of the vagina) or ulcers of a *tubercular* or *syphilitic* nature. The former correspond to those ulcers discussed further on as occurring on the vaginal portion of the cervix; the latter differ in no way from similar ulcers occurring in other parts of the body.

(C) HYPERTROPHY.

Hypertrophy affects either the stroma or the epithelium, as in prolapse of the vagina. Here there is a decided increase of the connective tissue and of the epithelium, which takes on an epidermis-like character; or there may be an epithelial hypertrophy, as in pointed condylomata. At times the vagina is studded with the latter. The anatomical picture is the same as that given for condylomata of the vulva.

(D) NEOPLASMS.

(a) Epithelial.

Under this heading only carcinoma is taken into consideration. It is primary only rarely, but frequently secondary through extension of a carcinoma of the cervix to the vagina. In its structure it resembles carcinoma of the skin and always originates from the squamous epithelium. It penetrates quickly into the surrounding tissue and changes the soft and dilatable vaginal canal into a rigid mass. The seat of the

carcinoma is usually upon one wall, especially the posterior, or it may surround the entire vagina like a ring.

(*b*) *Neoplasms of the Connective-Tissue Group.*

These are still more rare than carcinomata. Of the benign tumors, fibromata and fibromyomata have been described. As to sarcomata, it is to be especially remarked that they may occur in childhood. Microscopically they have the well-known forms—spindle-celled, giant-celled, and melanotic sarcomata.

(E) Cysts.

Cysts of the vagina lie directly under the squamous epithelium and rarely attain great size. Their lining is either squamous or cylindrical epithelium. Some contain ciliated epithelium. Concerning the origin of these cysts there is, as yet, no absolute agreement. The small cysts may, with reason, be considered glands abnormally present in the vagina, or may be viewed as cysts resulting from remnants of the Wolffian duct. The larger, on the contrary, which reach higher up and are found along the uterus, may positively be considered as the result of persisting Wolffian or Gärtner's ducts. (See Part III.)

Finally, lymph cysts may be formed from dilated lymph channels. The contents of vaginal cysts consist of a clear watery fluid; it may, however, become cloudy as a result of desquamation of epithelium.

III. THE NECK OF THE UTERUS (CERVIX UTERI).

We distinguish in the uterus the body or corpus, and the neck or cervix. The part which extends into the vagina is called the vaginal portion of the cervix, or *portio vaginalis.*

The cervix is perforated longitudinally by the cervical canal. This opens at the vaginal extremity as the external os, and above into the uterus as the internal os. Its walls are formed of strong muscle, which is covered externally by peritoneum. The external surface of the vaginal portion is covered by a continuation of the vaginal epithelium. Under it lies a small strip of connective tissue which may be viewed as the stroma of the vaginal portion. The connective tissue passes directly on into the muscular tissue, so that an anatomical line of division between the vaginal portion and the rest of the cervix does not exist. Such a division, as is made by some authors, cannot be carried out in practice, since, for instance, in making a test excision tissues of both parts are always removed. We consider, therefore, in the following discussion the neck of the uterus as a whole, consisting of the vaginal portion, cervical mucous membrane, and cervical stroma (connective tissue and muscle).

1. NORMAL ANATOMY.

The vaginal surface of the cervix is covered by stratified squamous epithelium which is the continuation of the epithelium of the vagina. Just as the latter is a continuation of the external skin and loses, where it becomes mucous membrane, the positive characteristics of the external skin, such as hair and glands, so there remains to the mucous membrane which covers this part of the uterus nothing but squamous epithelium. The existing papillæ are here so insignificant that we can scarcely speak

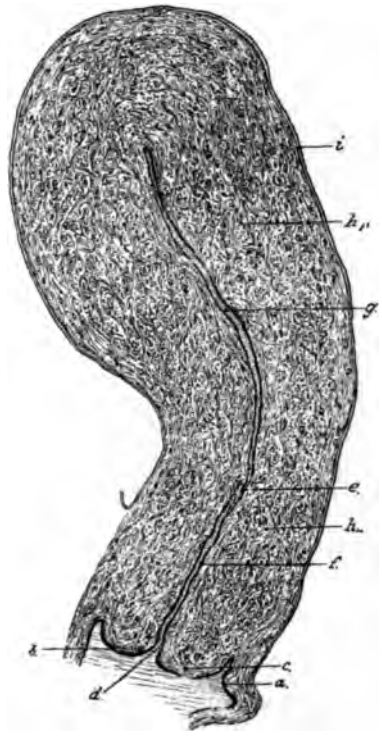

FIGURE 4.—LONGITUDINAL SECTION THROUGH A UTERUS.

a, vaginal mucous membrane; *b*, epithelium of the outer surface of the vaginal portion of the cervix (squamous epithelium); *c*, connective-tissue stroma; *d*, external os; *e*, internal os; *f*, cervical mucous membrane; *g*, endometrium; *h*, muscle tissue of the cervix; h_1, muscle tissue of the fundus; *i*, peritoneal covering.

of a real papilla. The underlying tissue is only loosely connected with the covering epithelium.

The papillæ are small, low, and rise only slightly toward the epithelium which covers the underlying tissue in an almost straight line.

The squamous epithelium consists of several layers which are like those of the external skin. Horny cells are absent; the uppermost layer is formed of flattened, sometimes fusiform, elements. The projections are rarely seen in alcohol specimens. Under these come the cells of the

rete Malpighii, which consist of the well-known large squamous epithelial cells (prickle cells). It may be considered, in general, that the squamous epithelial cells of the vaginal portion are smaller than those of the external skin. The lowest layer, which forms the boundary between the squamous epithelium and the stroma, shows low cylindrical cells with relatively large nuclei. This is the so-called formative layer (stratum germinativum), from which the thrown-off cells of the upper layers are replaced by new ones.

FIGURE 5.—VAGINAL SURFACE OF THE CERVIX UTERI.

a-d, squamous epithelium; *a*, layer being cast off; *b*, spindle-shaped cells (stratum granulosum; *c*, rete Malpighii; *d*, stratum germinativum; *e*, capillaries; *f*, fibrous connective tissue with nuclei; *g*, veins; *h*, arteries (longitudinal section); *i*, arteries (transverse section).

The tissue under this epithelium consists, in its upper part, of connective tissue rich in cells, while the deeper layers are formed by the muscular tissue radiating from the corpus uteri. As a rule only the nuclei of the connective tissue are visible, while the cell boundaries are seen with difficulty. Therefore, some authors call it a connective tissue "rich in nuclei."

Glands are normally not present in this stroma, only capillaries, arteries, veins, and sections of lymph vessels. According to recent investigations, numerous elastic fibres are present.

The arteries are remarkable for their relatively thick walls and for the strong development of the intima, wherefore they impress the inexperienced as being glands.

The squamous epithelium covers the external surface of the vaginal portion up to the external os, and only in rare cases passes on into the cervical canal. Here it changes to a simple ciliated cylindrical epithelium. Since the cilia can no longer be seen in the sections, we will speak of these cells as cylindrical epithelium, just as in Fig. 6, *c*, no cilia are to be seen.

The point of junction of these two forms of epithelium is not a certain one; sometimes it is situated high up in the cervical canal, at

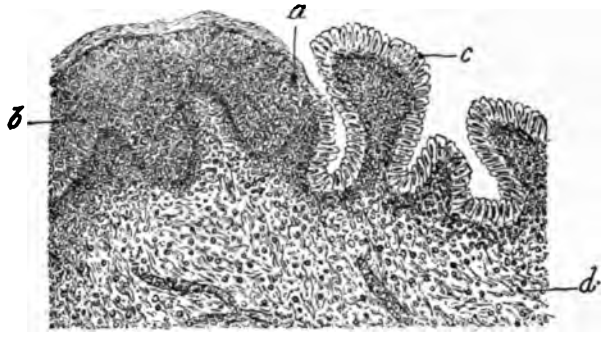

FIGURE 6.

Transition *(a)* of the squamous epithelium *(b)* of the portio vaginalis to cylindrical epithelium *(c)* of the cervical lining; *d*, stroma.

other times it is outside of the external os. As a rule this point of transition can be macroscopically recognized, for the surface covered with cylindrical epithelium lies rather lower than that covered with squamous epithelium. Besides, the color of the former is a lighter red. The transition may be gradual, the squamous epithelium becoming gradually thinner, or it may go over into cylindrical epithelium suddenly. By some authors a transition epithelium has been described.

The cylindrical epithelium covers the cervical stroma in an uneven line, and forms depressions, the well-known cervical glands. These are designed to secrete a glairy mucus which fills the cervical canal as a plug.

The glands do not extend very far into the underlying tissue, but their bottle- or balloon-shaped forms occupy only the upper part. The higher we pass in the cervical canal the more uneven is the surface of the mucous lining. The reason for this is that the stroma forms longitudinal folds toward the lumen of the canal, in this way narrowing it considerably. These folds begin at the internal os and extend toward

the external, forming the *arbor vitæ uterinus* or the *plicæ palmatæ*. In this way the surface is considerably increased in extent, and in transverse sections it may be seen that the tissue lifts itself in folds, with a deep depression between every two folds. Here the gland openings lie quite hidden, while upon the summit of the folds, as a rule, no glandular depressions are found. The lowest portion of the cervical canal is often free from glands, yet it cannot be considered pathological if they are present at the very beginning of the cylindrical epithelium.

The lumina of the glands have no regular round form, but are compressed by folds which project from the stroma toward the epithelium. In this way the cells of the opposing walls often approach each other so closely that no lumen remains.

The epithelial cells have a long, transparent protoplasmic body

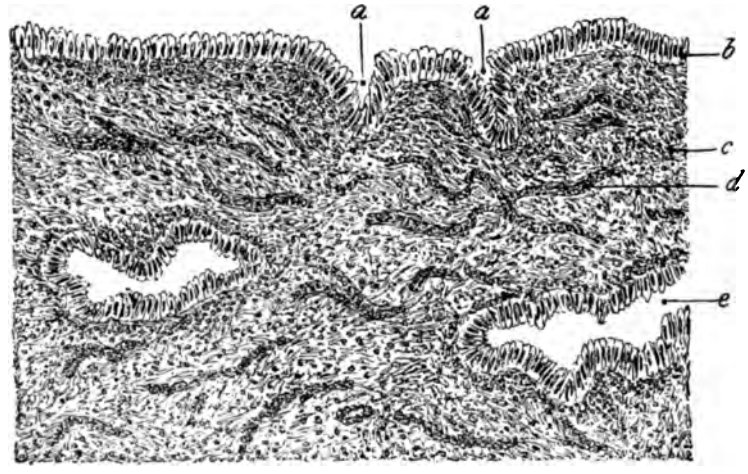

FIGURE 7.—CERVICAL MUCOUS MEMBRANE.

a, gland openings (cut obliquely); *b*, cylindrical epithelium (ciliated); *c*, connective-tissue stroma rich in cells; *d*, capillaries filled with blood; *e*, oblique section through cervical glands.

narrowing toward the base. The nucleus, which is small in proportion, is situated at the base. The cilia can be found, as a rule, only in the fresh specimen, examined in physiological salt solution immediately after removal. Through addition of caustic potash ciliary motion may be again excited.

The stroma of the cervix consists of connective tissue rich in cells only in the layers directly under the epithelium. The main constituent of its wall is formed by muscle fibres into which the fundi of the glands project. Next to the muscular tissue is the paracervical tissue, loose connective and fat tissue.

So much for the normal anatomy of these parts. There remains to be considered only the topographic condition of the glands situated near the boundary of the squamous epithelium. These do not run into the

tissue at right angles to the surface, but often make a bend under the surface and lie parallel to the squamous epithelium in a longitudinal direction. If in such a case a vertical section be made through the surface covered with squamous epithelium, there will be found under it one or more sections of glands, which, however, are in no way pathological, for this apparent abnormal condition is caused by the manner in which the section is made and is not due to an increase in the glands. To determine with certainty to what part such a gland belongs, and whether it is a normal gland formation or a newly formed gland, the entire specimen must be cut in a series of sections, to follow the gland up to its excretory duct. Such a procedure is necessary only in exceptional cases. It serves, however, to remind us that in examining our specimens we are often liable to such illusions, ignorance of which may easily lead to serious error. This may be the more easily understood when we consider that just in the cervix two different forms of epithelium meet, each of which is liable to decided changes of form upon the slightest irritation. First one and then the other form of epithelium gets the upper hand; an extremely vigorous growth, *as a reaction to every irritation,* is a quality common to both. In addition there may be a varying increase in the glands. It is therefore especially advantageous to the beginner if he learns of the existence of such constantly occurring "illusion pictures" before he begins to consider pathological processes.

MICROSCOPICAL ILLUSIONS.

(A) In Sections through the Squamous Epithelium.

We are accustomed to study the squamous epithelial covering of a surface in transverse section. Drawings of the same are usually arranged so that the different layers may be distinctly distinguished. If the section is not quite perpendicular to the surface, but more nearly parallel to it, the section makes a strange impression, for we see no longer the various layers, but only some of them; and these not in profile, but from the surface. The epithelial extensions which occasionally run deeper into the underlying tissue are no longer cut longitudinally but transversely, and may be mistaken for masses of squamous epithelium, such as are sometimes found in carcinomata. The entire epithelial surface appears thicker, and this condition may be easily illustrated in the section through a pointed condyloma (Fig. 8).

In this affection we find a hyperplasia of the epithelium which grows in all directions, so that in a section the epithelial surface is cut sometimes vertically, sometimes obliquely, and sometimes parallel to the surface.

In the case of the vaginal portion also such irregularities of the epithelium occur, when in alcohol some of the parts of the specimen

shrink more than others, so that elevations and depressions are formed. In a somewhat oblique section islands of squamous epithelium may then be found in the stroma and easily lead to error; at least I have often observed that the inexperienced examiner considers such fields to be carcinomatous.

In judging a section it must be held in mind that the vaginal surface of the uterus which is covered with squamous epithelium runs an arched course and not in a straight line. If then the section is made through the curving part a portion of the epithelium is so cut that the

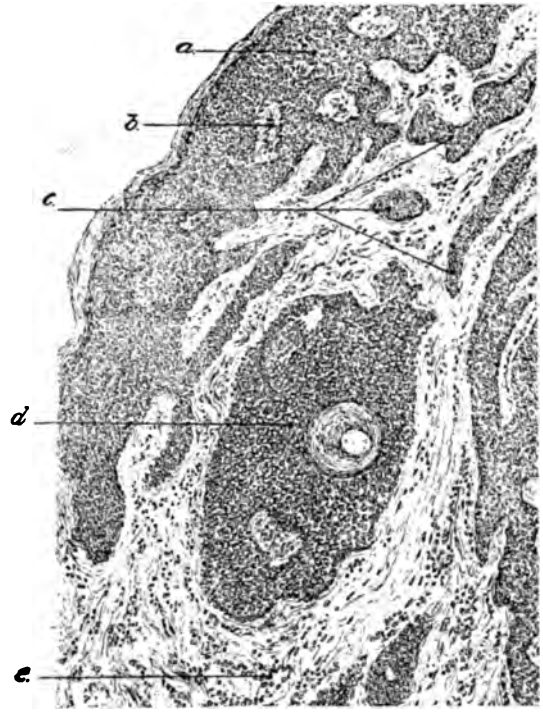

FIGURE 8.—SECTION THROUGH A POINTED CONDYLOMA.

a, squamous epithelium (oblique); *b*, oblique section of a papilla; *c*, islands of squamous epithelium, seen in various planes, showing at *d* an enclosed bit of the horny layer which resembles a cancer pearl; *e*, stroma infiltrated with small cells.

section is almost vertical, while the curving portion is, on the contrary, cut at a tangent, whereby the epithelium appears suddenly thicker and seems to penetrate into the underlying tissue.

For that reason, to avoid error one must carry in mind the appearance of sections cut in various directions. The beginner is therefore advised to purposely cut the specimen to be diagnosed in various planes. Even almost normal specimens then offer difficulties for the beginner if the line of cutting be unfavorably chosen. If at the same time pathological changes (inflammation, hyperplasia) be present, even a practised pathologist may have difficulty in making a correct diagnosis.

The chief criterion in deciding whether we are dealing with an oblique section or a pathological condition is the regular disposition of the epithelial cells to each other and the condition of the interstitial tissue; for if a malignant neoplasm penetrates into another tissue the latter does not remain unaffected, but reacts with a small-celled infiltration. There are then numerous lymphoid cells in the interstitial tissue, which take up the struggle against the neoplasm. In this way it is clear that a decision may be very difficult if the connective tissue for some other reason (inflammation) is already infiltrated with round cells. Then the regular form of the epithelial cells decides. A carcinomatous or sarcomatous neoplasm—in doubtful cases one of these is generally in question—does not contain regularly arranged cells of the same form, but distinguishes itself *through a multiplicity of cell forms.* In discussing carcinomata this condition will be considered more fully.

(B) In Sections through Glands Lined with Cylindrical Epithelium.

As in the case of squamous epithelium, drawings of glands are usually so made that the cylindrical cells are seen from the side. If the gland be cut longitudinally, a tube lined with cylindrical cells is seen; if, on

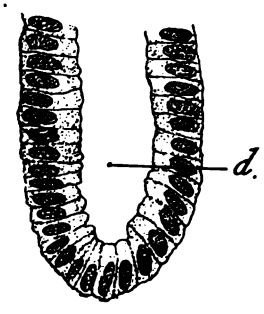

FIGURE 9.—*d*, LONGITUDINAL SECTION THROUGH A GLAND LINED WITH CYLINDRICAL EPITHELIUM.

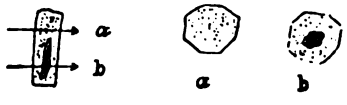

FIGURE 10.—TRANSVERSE SECTION THROUGH A CYLINDRICAL CELL (*a*, *b*).

a, beyond the boundary of the nucleus; *b*, nucleus also included.

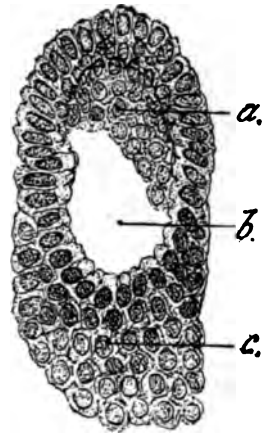

FIGURE 11.—OBLIQUE SECTION THROUGH A GLAND.

a, transversely cut cylindrical cells of a deeper layer; *b*, gland lumen; *c*, transverse or obliquely cut cylindrical cells resembling an epithelial proliferation.

the contrary, it be cut transversely, a circle is formed lined with cylindrical cells in profile. The cells then appear as longitudinal long cells with a large or small nucleus at the base.

The course of the gland is only in rare cases so simple and straight

that a section in all parts divulges a simple layer of epithelium, and this always in the same plane. Since, in addition, the uterine glands have a winding course, it is rare to see other than oblique or flat sections. In keeping with this result the cylindrical epithelia are not always seen in profile, but usually obliquely or from the surface; they then have no longer a cubical form, but appear broad, like squamous epithelium. Further, in a section a cell with or without its nucleus may be seen, according as the section includes the nucleus or not.

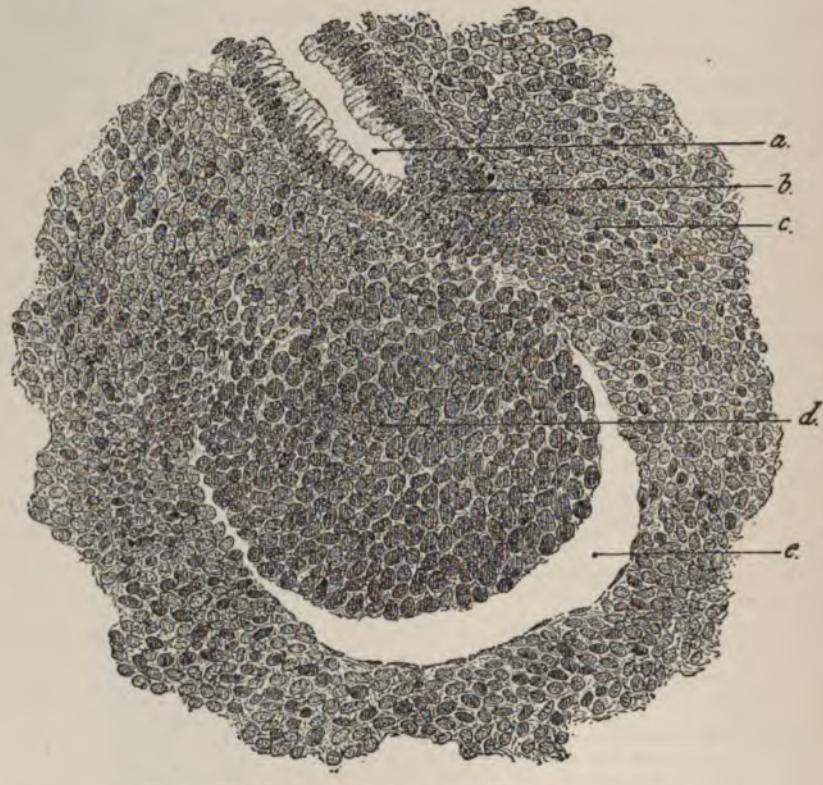

FIGURE 12.—SECTION THROUGH THE FUNDUS OF A GLAND.

a, gland lumen lined with cylindrical epithelium; *b*, horizontal section through the cylindrical epithelium; *c*, interglandular tissue; *d*, section through the gland fundus; *e*, space resulting from the greater shrinking of the epithelia in the alcohol.

A section not entirely vertical cuts the cells of the glandular wall in such a manner that on one side the cells are seen in profile, while on the other side oblique sections of the epithelium are seen. At the same time not only one but several layers of cells are seen in such an oblique section. This makes it appear as if the epithelium were in a state of growth, and may lead to erroneous diagnosis (Fig. 11).

While in oblique sections a lumen is always present, it disappears in a section through the fundus of a gland (Fig. 12). We see then only

the transversely cut cylindrical cells as a mass of epithelium lying in tissue, the entire picture resembling a carcinomatous alveolus. At any rate, I have frequently observed that beginners, and even practised microscopists, confuse these two conditions.

The chief differences consist in the *regular arrangement and in the similarity of the cells.* By high magnification it may be distinctly seen that the transverse sections of the epithelial cells have polyhedral forms like the cells of a honeycomb. If the interstitial tissue is not otherwise altered, a decision as to the existing condition is not difficult, and may, with practice, be made with certainty. If, on the other hand, complicating inflammatory changes are present—and this is especially the case in the endometrium—not only is the interstitial tissue infiltrated with small cells, but in most cases there has been great irritation of the epithelium of the glands, which is then incited to growth and really lines the wall in many layers.

Between the epithelia round cells make their way, and if the section shows these altered conditions obliquely or from the surface it is evident that under such circumstances a correct diagnosis of the true nature is difficult, for through the strong small-celled infiltration the boundaries of the glands appear obliterated, so that it seems as if they no longer existed—a condition which is one of the chief characteristics in carcinoma.

In such a case all diagnostic means must be called into play to insure a correct diagnosis. This is possible if the course of the glands be followed in a series of sections. Further, attention must be paid to the division of the nuclei. The finer diagnostic points will be discussed in the chapter on the diagnosis of malignant neoplasms. It is naturally impossible to discuss all the possible errors; I can only call attention to this point and mention that illusions are to be avoided in judging microscopic pictures. At any rate, if this fact be always borne in mind, practice in diagnosing the pathological changes in these organs will serve to distinguish them from these so-called illusions.

2. PATHOLOGICAL ANATOMY.

The outer surface of the cervix, when seen with the aid of the speculum, appears covered with a moist, shining, bluish-red mucous membrane which possesses a smooth surface, and is, as we have seen, the continuation of the vaginal mucous membrane. Such an appearance corresponds to the microscopical condition observed in the previous chapter, and is never a justification for a test excision.

When, on the other hand, the mucous membrane does not cover the entire surface of the vaginal portion, but suddenly ceases, giving place to smaller or larger, very red, uneven, and lightly bleeding spots, we are dealing with a pathological state. This ulcerating surface lies some-

times below the level of the mucous membrane, sometimes it rises above the surface in the form of excrescences. Usually this affection is found near the external os and extends from here in varying extent toward the vagina, which in extreme cases may likewise be affected. It is rarely that the external os is surrounded by normal mucous membrane while the affection is found further away.

In general, we may say that the macroscopical appearance of these various ulcerating processes is no complex one. This is probably the reason why all these changes of the vaginal portion have been given the collective name "erosion." This name characterizes the external appearance in this affection, but does not define its nature, for an erosion means, in general, loss of the epithelium of a mucous membrane. Since it is impossible, with the naked eye, to decide whether a surface is covered with epithelium or has lost it, especially when this surface is inflamed, it is evident that the term "erosion" is often used when in an anatomical sense no such condition is present. Attention has been called to the insufficiency of this clinical title, but no other proposals have met with general approbation.

The differences in the morbid processes which possess a like macroscopical appearance make it impossible to select a uniform name which corresponds at the same time to the etiological and the microscopical condition, for very different causes may bring about a like macroscopical appearance in one or other of the pathological stages. It is to be regretted that the expression "erosion" has been chosen, for it tends to cause erroneous impressions; at the same time it is difficult to give up this nomenclature. We will, therefore, for the present, use this expression for the macroscopical appearance of the conditions to be described. In order that no confusion may result, it must be understood that this term expresses only the external appearance of the affected area, without making any statement as to the anatomical changes existing. How unsatisfactory this title is, or rather how false it is, will be seen in observing the simple inflammations of the vaginal portion; for here the surface appears macroscopically very red, like an inflamed tonsil, yet the squamous epithelium is entirely present. If it is desired to unite all these conditions of the vaginal portion under one name, it is only possible by choosing a title which expresses nothing more than the macroscopical appearance.

In the following discussion the individual affections of the vaginal portion will be given names corresponding to the microscopical conditions which they present.

(A) INFLAMMATIONS.

(a) Simple Inflammations of the Portio Vaginalis.

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l portion is relatively rare as a
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Gonorrhea may also cause such
the interstitial tissue gonococci

thing more than that an ulcer-
his healing takes place by pro-
of the ulceration until it covers
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picture resembles that of a new
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fact that just in the neighbor-
d small-celled infiltrations occur
netrating neoplasm. It is there-
necessary to consider the cause of such a strong small-celled in-

filtration in the vaginal portion and to remember that a primary inflammation of this part is rare. It is therefore advisable to hold a patient under observation, even though the first examination has disclosed nothing further, and after a certain period another test excision should be made, especially if the clinical symptoms show no improvement.

There is yet another point to be observed. If, because of a very marked small-celled infiltration, a suspicion arise that a neoplasm exists, the sections should be made very thin, for then we are often concerned with a carcinoma which has existed only a short time or one which shows an unusually rapid growth. Such carcinomata do not form large typical alveoli which may be recognized at the first glance, but occasionally three or four cells form a carcinomatous alveolus. If the small-celled infiltration is very decided and the section very thick, then the carcinoma cells disappear under the small-celled infiltration and may in this way be overlooked. On the other hand, if the sections are thin the epithelioid carcinoma cells are easily distinguished from the small round cells. In the course of an inflammation brought about by mechanical causes a complete removal of the epithelium of the vaginal portion may result, with consequent destruction of the upper layers of tissue and the formation of an actual ulcer.

(B) Ulcers of the Portio Vaginalis.

A real ulcer occurs relatively seldom on the vaginal portion. The anatomical character of such an ulcer is very similar to the conditions which we have observed under inflammation, with the difference, naturally, that the surface is no longer covered with epithelium. In the uppermost layers the small-celled infiltration is especially strong. Frequently, in addition to turgid capillaries, extravasations of blood are observed in the tissue. Finally, in accordance with the character of an ulcer, the products of degeneration are much more numerous than in a simply inflamed tissue. The diagnosis of a simple ulcer offers no difficulties if one only remembers that the surface of a carcinoma also frequently shows ulcerating degeneration, and that underneath an ulcer a carcinoma may exist.

The causes for the existence of a real ulcer on the vaginal portion, naming the rarer cases first, are the same as for ulcers in other parts of the body, namely, *syphilis* and *tuberculosis*. Concerning these two processes on the vaginal portion very few observations have as yet been made. Such reports concern only occasional cases. This is especially striking in the case of syphilis, since this affection causes a productive inflammation, and thereby the epithelial growths on the vaginal portion due to syphilis may greatly resemble the changes caused by carcinoma. This error is possible, since two different forms of epithelium unite on the vaginal portion, both of which have a great tendency to proliferation after relatively small irritation. In my opinion, examination in this

direction possesses a great anatomical interest and is of great importance for the clinical diagnosis and the differential diagnosis of the "early stage of carcinoma."

Even though, in considering an ulcer of the vaginal portion, these conditions must always be kept in mind, *purely mechanical causes* are the more frequent cause of their development. In prolapse, as well as from long-existing pressure of a pessary, such an ulcer may be formed. Since in prolapse decubitus ulcerations are not infrequently observed, a doubt may arise in such a case as to whether a carcinomatous ulcer is present. For that reason we will study such an ulcer more closely.

As a result of prolapse the cervix comes in contact with the outer air. This causes so decided an irritation that the squamous epithelium

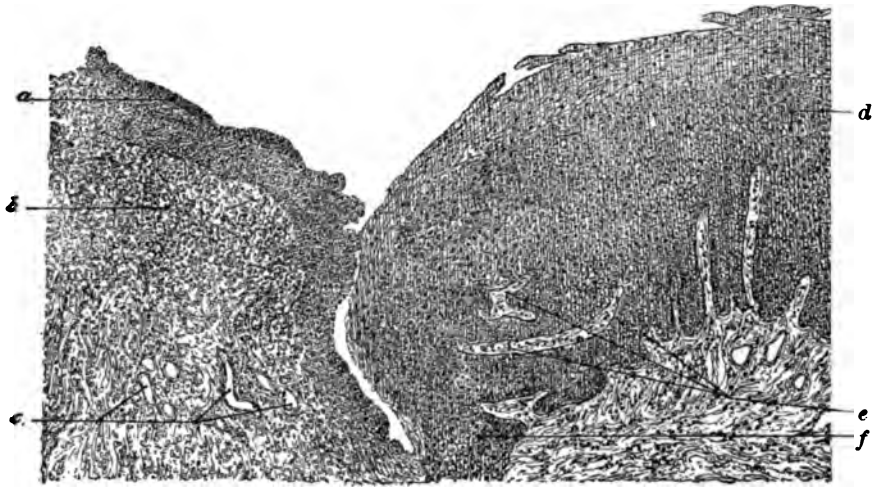


FIGURE 13.—DECUBITUS ULCER OF THE VAGINAL PORTION IN TOTAL PROLAPSE OF THE UTERUS *(f, end of the epithelium; to the left begins the ulcerating surface).*

a, ulcerating surface; *b*, small-celled infiltration of the stroma; *c*, capillaries; *d*, much-thickened squamous epithelium whose upper layers are being cast off; *e*, transverse and oblique sections through papillæ.

is increased to three or four times its normal thickness. This thickening appears, in a measure, to be an aid of nature in protecting the uterus from external injuries. Nevertheless, in many cases the epithelium is gradually thrown off through rubbing between the thighs, and actual ulcers are formed. If a vertical section through the surface of such an ulcer be made, we find, if an area of transition from healthy to diseased tissue has been selected, a small-celled infiltration under the epithelium in the neighborhood of the ulcer. This infiltration reaches its height in the areas entirely bare of epithelium, and at times extends far down into the tissues.

The deeper the ulcer penetrates, the more irregular is the surface and the more natural is a diagnosis, judging from its macroscopical ap-

pearance, of malignant neoplasm; for in these ulcers a symptom often of value in making the clinical diagnosis of carcinoma is present, namely, the easy bleeding on touch, either instrumental or through coitus. Since, however, the uppermost layers of such simple ulcerating surfaces, deprived of epithelium, are filled with numerous turgid blood vessels possessing only thin walls, the free bleeding when touched is easily understood. It may also be mentioned that these ulcers are only in the rarest cases the starting point of a carcinoma. On the contrary, as soon as the injuring cause is removed they readily heal.

(c) Ectropion and Inflammation of the Cervical Mucous Membrane.

As was seen in reviewing the normal condition, the stratified squamous epithelium of the vaginal portion borders on the cylindrical epithelium of the cervical lining with its glandular depressions. In the virginal uterus the boundary between these two forms of epithelium lies sometimes higher, sometimes lower in the cervical canal. At any rate, the outer surface of the uterus is normally never covered with cylindrical epithelium. This condition is different as soon as one or more births have occurred, for after these the external os is generally torn so that it gapes more or less according to the depth of the tear. In this way the previously invisible mucous lining of the cervix appears on the outer surface, while the part covered with squamous epithelium is forced back toward the fornix. In this manner cylindrical epithelium occupies the position previously taken by the squamous cells, and the so-called "ectropion" results. This appears (in a multipara a relatively normal condition) as an extremely red area in place of the normal blue and shining vaginal portion, and the numerous glands with their uneven surface give this condition an ulcerating appearance. This impression is still stronger if external irritation or congestion or a pregnancy makes the blood supply greater and gives the surface a dark-red appearance. This picture is still more characteristic, and its appearance is more like that of an ulcer, if in addition inflammation be present. The complicating increase of blood supply, and the infiltration of the tissue with lymphoid cells, may cause a very decided swelling of the cervical mucous membrane. This may be so decided that the cervical lining, welling out of the external os, rests upon the outer surface of the cervix like a fungus.

The microscopical changes found in inflammation of the cervical mucous membrane hold good for the everted mucous membrane as well as for the non-everted.

The stroma is infiltrated with small cells; the vessels, especially capillaries, are filled with blood. The glands, as a rule, are not changed in the early stages, but in certain areas leucocytes may be found between the epithelial cells. As may be readily understood, this stage is rarely observed microscopically, examination being usually made when the pro-

cess is more advanced and when great changes have resulted through chronic inflammation.

Then, in the first place, the glandular structures demand our attention. As a result of the continued excessive plethora, perhaps through the irritation which causes the inflammation, hyperplasia of the glandular epithelium results. This is evidenced either by a growth of the epithelial cells inside the glands, or in an increase in size and number of all the glands.

If the latter be the case, we see the glands forming the chief element of the tissue, while the interstitial tissue is more and more displaced by them. The glands, increased in number (hyperplasia), are situated close together, but preserve their epithelium and their glandular form without change. Besides, this growth caused by inflammatory processes remains confined to the superficial layers of the mucous membrane.

In case of enlargement (hypertrophy) of the glands they increase considerably in length and size. In some cases, although they are normally only depressions of the cervical epithelium, they may pass through the entire thickness of the vaginal portion up to the squamous epithelium, where they sometimes lift the latter off entirely. Through a coexisting proliferation of the connective tissue the glands possess no even calibre, but are narrowed by projecting folds. These may lie so close together that a canal is scarcely present. The cells of the opposing sides are in contact, and may even unite. Since the irritating cause increases the secretion of the epithelial cells, and since the narrowing of the gland lumen permits no sufficient outflow, an excessive dilatation of the glands may result. These may in the course of time be cut off from their ducts and form cysts.

The clinical symptom of such a condition which may lead to test excision is frequent, irregular bleeding with purulent discharge. If the microscopical picture corresponds to the above description, no doubt should exist that we are dealing with a benign formation.

It is different when an inflammation causes a hyperplasia of the glandular epithelium alone, for then the glands are no longer lined with a single layer of epithelial cells, but the latter are found in three or four layers. It may happen that the cells lose their cylindrical shape through pressure and become flat. If then an oblique section should be examined the sections through these flattened cylindrical cells look like squamous epithelium, and the impression is easily made that the gland lumen, partly filled with epithelia, is a carcinoma in a very early stage. Although we readily grant that such microscopic pictures require great care in judging a pathological process, we state that it is *absolutely incorrect to make from this condition alone the diagnosis of a "beginning carcinoma,"* for from the above description it may be seen that such epithelial growth within a gland may easily be the result of inflammatory changes.

Nevertheless it is to be recommended that such cases be carefully

watched and that new test excisions be made at regular intervals, providing, naturally, that the clinical symptoms, such as bleedings and discharge, do not disappear after continued treatment.

With what little right a beginning carcinoma would be diagnosed from such conditions, the following case observed by me may serve as an example. Fig. 14 gives an illustration of the same.

FIGURE 14.—TEST EXCISION FROM THE VAGINAL PORTION AFTER MUCH CAUTERIZATION.

Benign growth of epithelium in a gland. Epidermization of the surface. On upper side, to the right, a gland enters into the tissue and is cut obliquely. Below, to the right, are retained cylindrical cells in the gland otherwise filled with squamous epithelium.

The patient came to my clinic for uncontrollable bleeding from which she had suffered for six weeks, during which time she had been under medical treatment and observation. The "erosion" was cauterized by her physician with crude pyroligneous acid. As the bleedings did not cease, he performed a curettage, and at the same time made a test excision, since the vaginal portion looked suspiciously like carcinoma. His

examination of the excised piece led to no diagnosis, for it was too small and was spoiled in preparation. In spite of the curettage the bleedings continued, and the vaginal portion was treated exclusively with chloride of zinc, at first in weak and then in stronger solutions daily up to fifty per cent. The result was that the bleedings became stronger and actually intense when she came into my hands. Examination showed the vaginal portion to be strongly granulated and ulcerated; it bled on the slightest touch, so that macroscopically it had the appearance of a carcinoma. After the above history, however, it seemed advisable to attribute its appearance to the above mentioned cauterization. Still, I considered it advisable to make a test excision, with the microscopical result shown in Fig. 14.

Without doubt this condition could justly be called a "beginning carcinoma." Since the irritation of the long-continued treatment and the repeated surgical steps appeared to me sufficient to explain this decided growth of epithelium, I treated the patient with a simple gauze tamponade and absolute rest. After a few days the bleeding ceased and the patient recovered quickly from the loss of blood. Menstruation returned regularly upon the use of extract of hydrastis. On seeing the patient, after a lapse of six months, she was in perfect health, menstruation was regular, and the vaginal portion was of normal appearance. May this case serve as an example of a large category! At any rate, it furnishes proof that a diagnosis of carcinoma should not be too hastily made. *It is necessary to remember that in every inflammation hyperplasia of the epithelia may occur, and the pathological process must be judged accordingly.*

(D) "EROSIONS" (EROSIO EPITHELIALIS SUPERFICIALIS).

After having discussed real ulcers of the vaginal portion, the following division deals with those conditions which are frequently found, and which have occasioned the calling of all very red-looking changes of the vaginal portion "*erosions.*"

This condition is characterized by the fact that the vaginal surface of the cervix, which normally is covered with squamous epithelium, shows the presence of cylindrical epithelium to a greater or lesser extent. This causes a great resemblance to *ectropion* and a distinction microscopically between the two is often impossible. This is possible macroscopically only when an erosion occurs on the cervix of a nullipara or a virgin. Then the bluish-red, normal epithelial covering is substituted by a deep-red surface which, as a rule, surrounds the external os. At times, yet comparatively rarely, such areas occur far from the external os. These are sharply outlined from the surrounding mucous membrane; sometimes they lie at a deeper level. The change in the vaginal portion varies according to the extent of the affection. In advanced cases the macroscopical appearance shows such a torn, uneven, granular

character that carcinoma is immediately considered. If, in addition, such a surface bleeds easily on touch, then without doubt a test excision is justified. In microscopical specimens it is seen that, in place of squamous epithelium, cylindrical epithelium is present. There is, therefore, no complete loss of the surface epithelium, and an "erosion," in the pathological-anatomical sense of the word, is not present.

FIGURE 15.—A SO-CALLED "EROSION" OF THE VAGINAL PORTION *(section showing transition from cylindrical to squamous epithelium).*

a, squamous epithelium, interrupted at *b* through pressure of the vulsellum; *c*, cylindrical epithelium as covering of the surface usually covered with squamous epithelium; *d*, glandular depressions extending far under the squamous epithelium; *e*, stroma infiltrated with small cells.

The stroma shows in most cases slight changes. In spots there is a small-celled infiltration of slight intensity. The surface is covered with a simple cylindrical epithelium; I have never observed cilia. This epithelium covers the stroma in parts evenly, in parts it forms slight depressions into the underlying tissue. As a rule, glandular-like structures are found in the stroma, *i. e.*, transverse and longitudinal sections of tubes lined with simple cylindrical epithelium, which in general is lower

than that of the cervical glands and shows no cilia. This stage of the affection has been called "*simple erosion*" so long as only few glandular structures are present in the stroma. If, on the other hand, the cylindrical epithelium passes deep into the stroma, and then rises again to its original level, papillary structures are formed which in the gynecological-anatomical literature are called "*papillary erosions.*" If the surface is smoother, and if at the same time there are more epithelial depressions, the condition is called "*follicular erosion.*" These expressions only confuse the beginner, since "papillary" and "follicular" are already confined to other conditions; especially is this the case with the word "papillary." It is always difficult to make the beginner, who has pursued anatomical studies, understand that in this branch of pathological anatomy we are not dealing here with real papillæ. In addition, among the above-mentioned three subdivisions of "erosion" no one form is exclusively present, but the various divisions run into each other. It would be best, in my opinion, to accept for general use the title adopted by me. "*Superficial epithelial erosion*" *signifies a condition in which cylindrical epithelium is present on the surface of the vaginal portion normally covered with squamous epithelium. This continues, sometimes deeper, sometimes not so deep, into the stroma, in which at times few, at times very numerous, gland-like structures may be present* (Fig. 15).

The stroma shows small-celled infiltration in the early stages of this condition. After a length of time the changes in the stroma may disappear without leaving any traces, and there remains then only the epithelial change. The characteristic of this so-called "erosion" is that in a stroma which, in the normal condition, is free from glands,[1] glands result through an unknown irritation with an isochronous substitution of the covering squamous by cylindrical epithelium. This change is clearly expressed by Orth,[2] who says: "The most important and interesting point is the presence of glands similar to those occurring in the normal lining of the cervix, so that we might say that, in place of the vaginal mucous membrane of the vaginal portion, cervical mucous membrane is present, showing, however, productive inflammatory changes."

When erosions are present for a long time—they are generally chronic affections—there may occur in the stroma and in the epithelium all those changes which we have learned in the previous chapter on inflammation of the cervical lining, therefore those conditions may be added here.

I should like to discuss briefly the origin of these erosions. It must be mentioned that all these explanations are only hypotheses. In the first place, it must be granted that an irritation may cause the cervical epithelium to proliferate; that this growth of epithelium displaces the squamous epithelium and leads to increase, *i. e.*, a new formation of

[1] Comp. Normal Anatomy.

[2] Text Book of Special Pathology, p. 438.

glands. In most cases, in fact, a cervical catarrh is present. It may be supposed that this continuous discharge of pathological secretion macerates the squamous epithelium, which is finally thrown off and replaced by the cervical epithelium engaged in proliferation. This locally displaced epithelium forms here, as it does in the cervix, glandular depressions. The presence of glands or gland-like formations has therefore no special meaning, but is, in a certain way, physiological.

It may be mentioned that in nearly all organs whose surface is covered with ciliated or simple cylindrical epithelium, glandular formations are found. This explanation is not true in a series of cases, for it can be observed that catarrhs with irritating purulent secretion exist without the least affection of the covering of the vaginal portion of the cervix, and *vice versa.*

Here Fischel's interesting observation concerning "congenital histological ectropion" furnishes an explanation of the substitution of one form of epithelium by the other. He believes, namely, that in the newly born the outer surface of the vaginal portion not infrequently has a cervical structure. Either in the future this "infantile habitus" persists, or in the process of development the squamous epithelium makes its way over the surface without the disappearance of *all* the cylindrical elements. One may then imagine that an irritation is sufficient to stimulate the latter to growth and to the formation of an erosion. At the same time, Fischel's theory furnishes an explanation of those cases in which the "erosion" is not closely connected with the cervical mucous membrane, but forms isolated islands surrounded by squamous epithelium and covered with cylindrical.

According to another theory[1] the cylindrical surface epithelium, as well as its depressions into the stroma, originates from the stratum germinativum of the rete Malpighii. The upper layers of the squamous epithelium are then thrown off during this affection, while the formative layer remains as an independent covering of cylindrical epithelium. In some cases this may be true; yet it is a theory rather more far-fetched than the other, for why should this layer of the stratum Malpighii, which usually forms only squamous epithelium, suddenly be employed in forming cylindrical epithelium? I have discussed these erosions fully, because they play a decided rôle since we have learned to make test excisions of the cervix for microscopical examination. In particular it may be mentioned that malignant neoplasms are supposed to originate from them.

According to Orth there exists a carcinomatous erosion. This assertion, first made by Ruge and Veit, is in my opinion not proven, but is likely to lead the beginner to make a diagnosis of early glandular carcinoma when in reality only a benign epithelial hyperplasia is present. I refer the reader to the discussion concerning such hyperplasia under

[1]Ruge and Veit.

inflammation of the cervical mucous membrane. By this I do not deny that carcinoma and erosion may be coexistent. My continued examinations have taught me that just in the areas which macroscopically look suspicious, and in which the so-called "erosion" glands were present, as a general rule no carcinoma is found. If the latter is present, then, on the contrary, the surface is really ulcerated, and an enormous small-celled infiltration of the stroma is present without gland formations, and *we have a typical carcinoma originating from the squamous epithelium.*

(B) NEOPLASMS.

In contrast to the changes previously described, in which there is more or less loss of substance, we are to concern ourselves in the following paragraph with those conditions which lead to partial or total growth of the individual elements of the cervix. These neoplasms are clinically either *benign* (hypertrophy, hyperplasia) or *malignant* (carcinoma, malignant adenoma, sarcoma).

The advanced cases of the first kind are usually so well characterized that with clinical experience a correct diagnosis may usually be made without previous microscopical examination. As a rule, we have here circumscribed growths which must be removed *in toto.* It is different when the cases are viewed in their early stages. Here we operate, as a rule, without previous test excision (except when carcinoma is suspected, when I advise a diagnostic test excision); but we must never omit a subsequent microscopical examination of the extirpated tumor, for *even in inoffensive-looking polyps destructive processes may occur,* which after diagnosis compel the performance of a major operation instead of the simple removal of the polyp. Since, on the other hand, even under benign neoplasms microscopical pictures are found which the beginner may view as carcinoma, I consider it necessary to describe these changes before passing on to malignant tumors.

1. Hypertrophy of the Outer Surface of the Vaginal Portion.

The benign hypertrophies of the vaginal portion involve either the *epithelium* or the *muscular structure,* or both. They may lead to diffuse growth of these parts, and are then called hypertrophies of the cervical lips *(elongatio colli).* If, on the other hand, only individual parts of the matrix go on to excessive growth, there result polyps of the outer cervical lips.

(a) Hypertrophy of the Epithelium.

This is most frequently observed in

(α) Prolapse.

A peculiar change in that part of the uterus projecting from the vagina is caused by friction between the thighs, and by irritation through

the air from which it was previously protected. This concerns exclusively the epithelial covering, and it is observed that the original moist, velvet-like polish and the red color have disappeared and given way to a dry tissue and a grayish color. This change is the result of an enormous hypertrophy of the epithelium. In place of four or five layers, twenty to thirty appear, the uppermost of which have the character of the horny layer of the external skin and are constantly in a state of desquamation and regeneration. The papillæ, originally scarcely to be observed, enlarge greatly and form wide elevations, sometimes slight prolongations of the stroma, which penetrate the entire layer of pavement epithelium. The mucous membrane is, in fact, made into epidermis. This condition resembles exactly the external skin, with the absence, of course, of the special elements of the same (see Fig. 13).

In most cases the line of division between this thickened epithelium and the underlying tissue is distinct. It happens, however, if the prolapse has existed for years without treatment, that the epithelial cones lying between the papillæ grow deeper and infiltrate the upper layers of the stroma in network form; we then have an "atypical growth of epithelium," according to Friedländer. Such a genuine growth of epithelium is very rare in this part. On the other hand, in hypertrophy of the epithelium illusions are easily produced in certain sections which easily give the impression of a real "atypical growth of epithelium"; for when the section is not made perpendicular to the surface, but obliquely or at a tangent, then those specimens in which the base of the papillæ is cut transversely or obliquely show a remarkable picture containing isolated epithelial masses and transversely cut papillæ. The practised eye recognizes *from the arrangement of the cells, from their normal relation to each other, and from the condition of the other tissues,* whether a neoplasm or an oblique section is under observation; to the inexperienced a proper diagnosis of such sections causes great difficulty. Facts teach us *that it is rare, very rare, that these epithelial hypertrophies in prolapse lead to carcinoma.* On the contrary, it seems as if this firm epithelial armor furnishes a splendid protection to a prolapsed uterus which is especially liable to irritation. At least I have never seen a carcinoma result from these benign epithelial hypertrophies in prolapse. It is, however, not impossible that a carcinomatous uterus may prolapse, or that a prolapsed uterus may occasionally become carcinomatous.

Of the partial hypertrophies of the mucous membrane on the outer surface of the *portio* must be mentioned

(β) Condylomata Acuminata.

The pointed condylomata, as is known, occur most frequently upon the external genitalia as a result of gonorrhea, and as a rule are confined to those parts. Nevertheless it is observed that at times they extend further into the vagina and give it an irregular surface, which bleeds easily on touch. In rare cases they extend up to the *portio vaginalis*

and form there the well-known warty excrescences, especially during pregnancy. These would have no further interest, from the standpoint of examination, if they always showed a typical appearance and if we knew the previous history. Even on the external genitalia it is not rare to find that several pointed condylomata have united into a tumor the size of a hazel-nut, forming a mass which has an ulcerating surface, bleeds easily, or discharges a purulent secretion. This makes the diagnosis difficult, and the same thing occurs upon the cervix. Here, however, greater difficulties in recognizing the affection arise, for the process on the external genitalia and in the vagina may have run its course, while it persists on the vaginal portion only. We then see not only a tumor with an ulcerating surface, but one which projects above the surface of the *portio,* which is hard to the touch and bleeds easily. A coexisting gonorrheal urethritis is, of course, no proof of the nature of the tumor on the cervix. Therefore a microscopical examination alone can make a diagnosis positive. In excising the tumor one must not fail to remove the matrix of the vaginal portion of the cervix likewise, in a wedge-shaped piece, and to make the excision so that a portion of the normal mucous membrane is included. The resulting wound is easily closed with a suture. This test excision is therefore rather extensive, but the procedure is harmless, and the advantage for a positive diagnosis is decided.

In a section made through the entire tumor perpendicular to the surface, it will be at once seen that we are dealing with a harmless epithelium *which shows no tendency to penetrate deeply.* The entire tumor is caused by an enormously increased formation of squamous epithelial layers, which rest upon the numerous branched papillæ like a fungus. These branches make it possible that an ideal vertical section cannot be obtained. The papillæ and the squamous epithelium are then seen in the sections in every possible plane (see Fig. 8). It has already been mentioned in the paragraph on "Illusions" that in this manner illusions may result to the unpractised eye, and that a horizontal section through epithelium surrounded by other tissue may easily be mistaken for a carcinomatous alveolus. I repeat again that the normal arrangement and the normal appearance of the cells of the squamous epithelium is an all-important factor in judging a section. This is especially to be observed when only a small piece has been removed for examination. If, on a section through the entire tumor surrounded by normal tissue, this tumor be seen elevated like a fungus *without penetrating into the deeper lying structures,* there is no doubt that we are dealing with a benign epithelial neoplasm, no matter how large the latter may be. If the condyloma be ulcerated, this surface has the appearance which we have studied in discussing the true ulcers of the vaginal portion.

(b) Hypertrophy of the Stroma.

This is in some cases a *diffuse* hypertrophy, *i. e.,* one or other of the

lips of the cervix, or both, become hypertrophic, whereby a decided lengthening and thickening takes place (cervix hypertrophy, *elongatio colli*). In other cases there is only a *circumscribed hypertrophy* of certain areas, a so-called "polyp."

(α) Elongatio Colli.

In hypertrophy of the cervix all the elements forming this part are affected. A microscopical section contains all those elements which we have learned in viewing normal conditions. Most noticeable is the enormous increase of the fibrous connective tissue, which may occupy the entire field. Hand in hand is an enlargement of the vessels which in some cases is decidedly surprising. The cellular elements of the connective tissue are least represented; these probably are destroyed through the pressure of the newly-formed connective tissue. What the causes for the development of such an unusual growth may be has not been determined. It may become so decided that the cervix projects as far from the vulva as in a completely prolapsed uterus. An elongation would of itself have no further diagnostic interest, were it not that, as a result of the protrusion of the cervix from the vulva, the same ulcers may develop as in prolapse. Through the coexisting hypertrophy of the connective tissue the presenting part often feels as hard as stone. This, in conjunction with an easily bleeding ulcer which produces fetid secretion, makes it impossible to say at first whether a carcinoma is or is not present. It is therefore necessary, before taking any operative steps, to make a test excision.

The ulcers, as well as the epithelial covering of the non-ulcerated parts, resemble those found in prolapse. Yet even among these hypertrophies carcinomatous ulcers have been reported. I myself have as yet not had the opportunity of observing such.

(β) Cervical Polyps.

To avoid any misunderstanding as to what is understood by cervical polyps, I should like to give an exact definition of the same. Literally, cervical polyps are polyps of the neck of the uterus. That under polyps we mean pedunculated growths (*i. e.*, only the form is described), requires no special mention. A polyp may possess a thin pedicle of various lengths formed by the tissue matrix, or may be attached by a broad base. In either case the pedicle must be well defined from the matrix from which the neoplasm issues. For that reason we must make a sharp distinction in the cervix between absolute growth (elongation of the cervix, cervix hypertrophy) and partial growths (cervical polyps).

Anatomically three forms of polyps may be distinguished in the vaginal portion of the cervix:

1. Polyps originating from the external squamous epithelial surface of the cervix.

2. Those which are formed at the junction of the squamous and cylindrical epithelium.

3. Those which originate in the cervical canal and, therefore, from a surface covered entirely with cylindrical epithelium.

According to its origin such a cervical polyp has as a covering squamous epithelium or cylindrical epithelium, or both.

Corresponding to its epithelial covering, a polyp possesses the stroma of that tissue from which it originates, and represents simply an excessive circumscribed growth of an existing tissue. Just as the elements normally present in the originating matrix are here represented, so likewise may be found in polyps such formations as are frequently found in the originating base of the polyp, without their being considered as serious pathological changes. In the cervix these are, as we have seen,

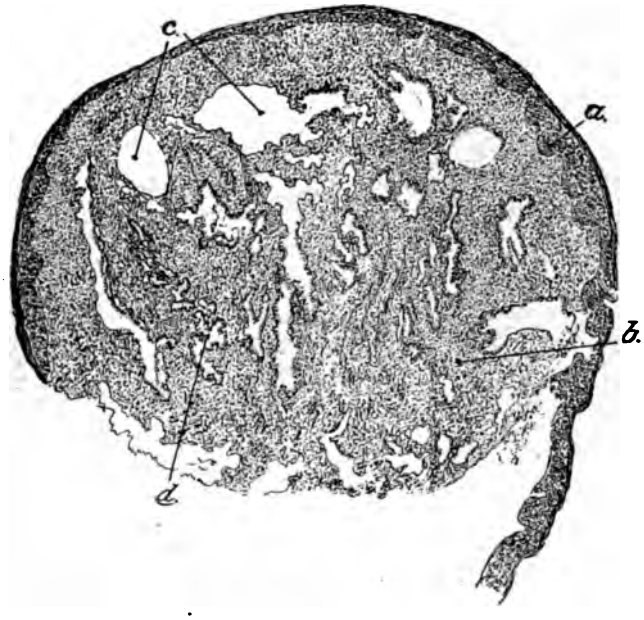


FIGURE 16.—POLYP OF THE CERVIX *(originating from the vaginal surface).*

a, squamous epithelium; *b*, stroma infiltrated with small cells; *c*, cystic spaces, dilated glands; *d*, spaces lined with cylindrical epithelium.

mainly glandular neoplasms. Therefore, if a polyp originates from the outer surface of the vaginal portion, it will show a covering of squamous epithelium if the area from which it originated was normal. In addition, it will consist of a stroma containing numerous connective-tissue cells, fibrous connective tissue, and vessels. The latter are especially well developed in the pedicle, so that here all the other tissues are in the background. The increase in the vessels is also present on the surface of a polyp, where turgid capillaries are often found.

From this we understand why such polyps bleed easily on touch, and why dangerous bleeding after removal of such polyps and secondary hemorrhage may occur, if the pedicle be not properly treated.

If in the stroma there be found spaces lined with cylindrical epithelium, this condition cannot be considered unusual in view of our explanations given above.

In the same way polyps which originate from the cervical mucous membrane may contain, like the latter, numerous glands as their main constituent. And since in polyps we are dealing with a process of hypertrophy, it follows naturally that these glands are partly enlarged and changed in form, and partly show a great increase in number. In some cases the polyp may consist almost entirely of glands with very little interstitial tissue (*adenoma polyposum*, or polypoid adenoma), so that it seems, on transverse section, cribrated like a sieve. In rare cases myxomatous degeneration of the connective tissue is observed in these latter forms, which causes the formation of a tumor called *myxadenoma polyposum*, or polypoid myxadenoma.

From the above description of their mode of origin, it is clear that no

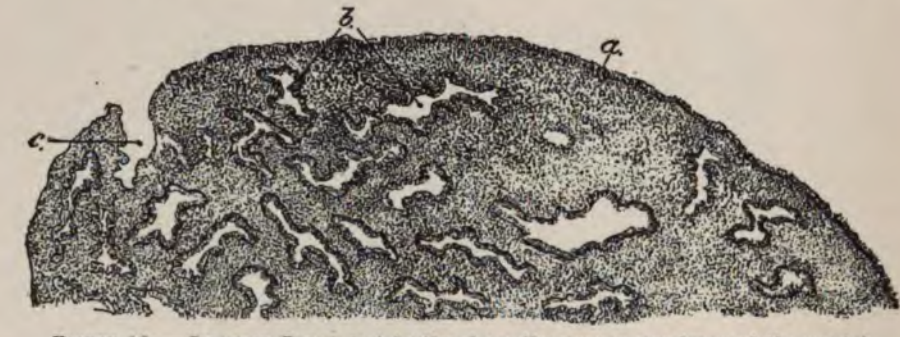


FIGURE 16*a*.—CERVICAL POLYP *(originating from the mucous membrane of the cervix).*

a, cylindrical epithelium of the surface; *b*, glands lined with cylindrical epithelium; *c*, glandular depression of the surface cylindrical epithelium (epithelia cast off).

great weight is to be laid upon the fact that one-half of the surface of a polyp may be covered with cylindrical epithelium, while the other half has a covering of squamous, for normally these two forms of epithelium border on each other. It would be fundamentally wrong if this condition in a polyp were to be judged otherwise than the same condition in the tissues from which it arises. The hypertrophy of the stroma of a polyp may naturally be imparted to the epithelium, and then the same changes result as we have learned may occur through irritation of the epithelium in prolapse and in the case of elongation of the cervix. A thickening of the epithelium may readily develop on the surface of a polyp covered with squamous epithelium, especially if the polyp is so long that it projects from the vagina. The projections of squamous epithelium may sink deeper than normally into the underlying tissue, without giving us the right to conclude, as is frequently done, that we are dealing with a "beginning carcinomatous degeneration of the cylindrical epithelium."

We now come to the special consideration of these polyps in a microscopic diagnostic relation. Every clinician has had the experience that such polyps, especially those which under the microscope are found to contain numerous glands, at times recur after simple removal. The *return of a neoplasm* is always a symptom not to be undervalued.

Since this question is important, I quote literally the remarks of two authors who have had great experience in this matter.

Gusserow says:[1] "The only symptom which these conditions (polyps) cause is bleeding—bleeding which at first follows the type of menstrua-

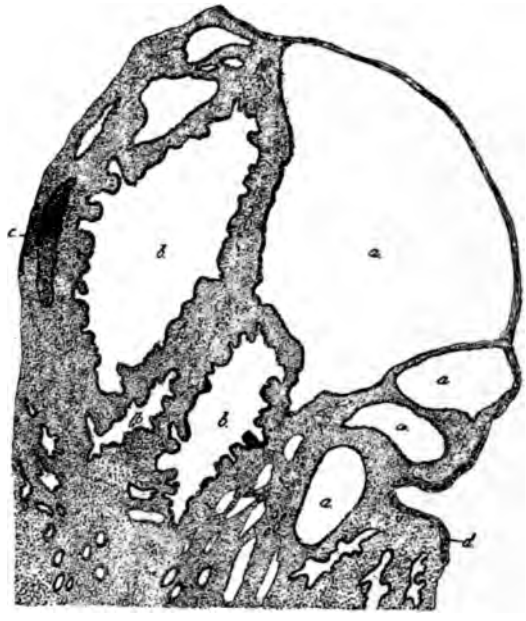


FIGURE 17.—CERVICAL POLYP.

a, cysts whose walls are partly lined with cylindrical epithelium and partly are deprived of epithelium; *b*, dilated glands; *c*, horizontal section through a squamous epithelial group; *d*, squamous epithelium which above is stretched very thin —numerous sections through vessels in a stroma infiltrated with small cells.

tion and is only characterized by the amount of the loss of blood, and later, lasting always longer, becomes a seemingly irregular bleeding, which in this way may lead to a high degree of anemia. What makes this affection, however, still more serious is its tendency to recur, as well as the undoubted fact that it leads, in a large number of cases, to carcinoma of the uterus, usually carcinoma of the body. Such observations have been made by Breisky, Schröder, Maslowsky, Winckel, Schatz, and others. From the cylindrical epithelium of the newly-formed glands growths extend into the lumen of the glands and into the stroma, and the glands are in this way filled with cells, and there occur in the deeper

[1]Billroth-Lücke: Text Book.

layers of the mucous membrane, and later in the muscularis, atypical cell groups in the glandular spaces. This course is the more to be feared the sooner after single or repeated removal of the adenomatous growths they return, and the nearer the individual approaches the climacterium or the further she has passed it."

Williams[1] expresses himself in a like manner:

"The polyp was 1.8 centimetres long, 1.25 centimetres wide in its greatest diameter, and had a thin pedicle. It was cut in its entire length and examined microscopically, whereby a remarkable and noteworthy condition was found. The lower and broader end of the polyp was covered with a layer of carcinomatous squamous epithelium, which *sent prolongations into the stroma of the tumor, and which penetrated several gland walls.* Above the point at which the carcinoma ended the surface of the pedicle was covered with cylindrical epithelium, in which numerous ducts of glands opened. The pedicle was perfectly normal.

"We were dealing, without doubt, with a mucous polyp which had arisen from the mucous membrane of the cervical canal. The deeper part, projecting from the external os, seems to have taken on squamous epithelium, while the remainder retained its original covering of cylindrical epithelium.

"Polyps of the uterus in an advanced stage have a tendency to become malignant, and therefore every one should be examined histologically as to its true nature after removal."

The fact that such polyps may become carcinomatous is to be considered as positive. The question is: what *positive* evidences do we possess to enable us to diagnose such a carcinomatous degeneration as early as possible?

Each of the authors whom I have quoted gives a different cause for the occurrence of carcinoma in these polyps. Either it originates from the surface epithelium or from the epithelium of the glands.

As we have seen, the cervical polyps are sometimes covered with the one and sometimes with the other form of epithelium, and sometimes with both forms. So long as a polyp is covered with cylindrical epithelium the occurrence of a carcinoma in it is very rare. It is different, however, with the squamous epithelium. It has long been known that squamous epithelium, as a result of irritations as yet unknown, forms growths and sends projections into the underlying tissue, which growths *penetrate into the glands and break through the vessel walls, without respecting the borders or limits of these tissues,* and, in a word, become a carcinoma. This diagnosis cannot, however, be made if the squamous epithelium is only, as compared with the normal condition, thickened, and if perhaps a few epithelial projections have really penetrated a little deeper into the stroma; for we have already called attention to the fact that associated with a polyp there is a general hypertrophy of all the

[1] Williams: Carcinoma of the Uterus.

formations naturally found in the tissue. We should therefore not be surprised if the squamous epithelium joins in this change and becomes hypertrophic. The conditions in this case are exactly the same as those which we recognize in that of prolapse and in elongation of the cervix. Nowhere else are so many errors possible; illusions are produced by the plane of the sections and easily give rise to error, for the polyps frequently show a very irregular surface, so that a section of the squamous epithelium may be vertical, oblique, or tangential. In the diagnosis of this condition special consideration must be given to this fact, and I therefore refer to the chapter on "Illusions." The criteria which we follow in making the diagnosis "carcinoma" will be fully discussed in the chapter on that affection.

In the same way mistakes may occur in making the diagnosis of glandular carcinoma; for it is just in hypertrophic formations that we find as a result of increased nutrition HYPERPLASIA OF THE CYLINDRICAL EPITHELIUM. This is shown by an increase of the glands or by a growth of the epithelium in the glands. It is not rare to find the gland spaces lined with three or four layers of cylindrical epithelium; yet it is incorrect to diagnosis a beginning carcinoma from this condition alone, because an increase of gland epithelium may be simply the result of a benign hyperplasia. That oblique sections, together with inflammatory changes which make the gland limits indistinct, may cause difficulty in diagnosis, requires no further special mention.

It may be seen from this discussion that in judging whether such a polyp has undergone carcinomatous degeneration or not great difficulty may be found. This can only be decided if a clear idea is had of what a true carcinoma really is, and if its appearance, and the fact that it penetrates into tissue affected by it, be remembered. To make these conditions clear is our next task. I should prefer, before closing this chapter, to emphasize again that we cannot be careful enough in the diagnosis of a "beginning carcinomatous degeneration."

2. CARCINOMA OF THE CERVIX.

The numerous anatomical works on carcinoma of the uterus which have been published in the last decade have not essentially advanced our knowledge of the nature of this affection, while, on the other hand, they have been of the greatest value in determining our present views as to its treatment. According to the microscopical examinations of Ruge and Veit, Schröder distinguished between (1) a *superficial cancer* of the *portio vaginalis,* which develops on the mucous membrane of the vaginal portion, and which has very little tendency to extend to the lining of the cervix, and (2) *carcinoma of the cervix,* which begins as circumscribed carcinomatous nodules under the mucous membrane, and then either extends to the outer surface of the vaginal portion or breaks into the cervical canal. From this Schröder formulated the axiom that in the

first case, so long as the carcinoma is confined to the vaginal portion, infravaginal amputation of the cervix should be performed, while supravaginal amputation should be performed so soon as the carcinoma has extended to the vaginal tissue. Recent investigations, on the contrary, have taught us that such a schematic division cannot be carried out, but that in *cancer of the vaginal portion carcinomatous changes occur in other parts of the uterus and pelvis much more frequently than was formerly believed.* When Schröder says that in the treatment of carcinoma

FIGURE 18.

b, carcinoma in a vein *(a)*, at some distance from the carcinoma centre; *c*, transverse section of an artery with very thick wall; *d*, tangential section through a vessel; *e*, muscular tissue.

of the cervix the important step is a radical removal of the carcinoma, we now understand by that statement *a total removal of the entire organ.* Even though the results, so far as recurrence is concerned, are still poor, *the cause of this is the fact that carcinoma is perhaps to be considered a local affection only in its earliest stages.* If it exist for some time, as is usually the case when the patients are made cognizant of it by certain symptoms, it is then impossible for us to say with certainty whether elements of the carcinoma have or have not already been carried further

through the blood or lymph channels, and these elements, in spite of the most extensive operation, MAY GIVE RISE TO A RECURRENCE in seemingly healthy pelvic tissues. I cannot refrain from mentioning an unusually characteristic case which came under my observation. A thirty-seven-year-old patient suffered ONLY TWO MONTHS from irregular bleedings and discharge. Local examination disclosed a carcinoma of the anterior lip of the cervix, which seemed to be confined to this area alone. Neither the vaginal wall nor the parametrium was affected or showed any signs of involvement. Total extirpation through the vagina was easily carried out in the absence of complications. As much as possible of the broad ligament was removed, *so as to be certain of having operated in healthy tissue.* The specimen was subsequently, as is always the case, subjected to close microscopical examination. It was found that far from the carcinoma, IN AN OTHERWISE HEALTHY-LOOKING AREA, a carcinomatous alveolus had made its way into a vein, as is clearly seen in Fig. 18.

This instance is proof again that one cannot operate too radically, and that it is certainly useless to remove only a portion of the uterus. The time is certainly near when the few partisans of partial extirpation will decide, as a result of anatomical facts, upon removal of the entire organ.

I should not have entered upon the discussion of these clinical conditions if the same were not of importance to the microscopist. At the moment at which we remove the entire uterus because of the microscopical diagnosis "carcinoma," it is no longer the duty of the microscopist to decide whether the carcinoma is only superficial (which is only possible in the very early stages) or is a deep cervix carcinoma. His duty is only to decide whether or not carcinoma is present; for if once the microscopical diagnosis "carcinoma" is made the therapeutic action of the clinician is indicated, namely, total extirpation of the uterus.

We will discuss in the following chapter the question as to when we are justified in making the diagnosis carcinoma, without discussing the finer anatomical questions, the mode of development, the channels of extension, etc.

Carcinoma of the cervix appears in two very different forms. Either it takes its origin from the *squamous epithelium* of the vaginal portion or from the *glands of the cervical mucous membrane,* and then destroys the neighboring tissues, especially in the latter instance, before it penetrates to the outer surface.

In the first form the carcinoma has a decided tendency to *ulceration,* so that we may with justice speak of a *carcinomatous ulcer.* In viewing the cervix through the speculum we see in these cases, as a rule, a very red irregular surface which bleeds readily when touched with the sound. Sometimes one lip, sometimes both lips of the cervix are affected. In contrast to the usual form of ulcers, the ulcerating carcinomatous surface *does not lie below the surface* of the cervix, but *projects* above it

(not to speak of those cases in which a large tumor partly fills the vagina). When the neoplasm has grown to the latter extent, no microscopical examination is necessary in order to form a diagnosis, for here our clinical experience is quite sufficient. It is different when we are dealing with a *beginning carcinoma of the cervical canal,* for here the appearance through the speculum *does not necessarily show any change.* The squamous epithelium covers the surface as in normal cases, so that on inspection we seem to be dealing with a healthy organ. Here the history of the case and *palpation* are of decided value, for usually the examining finger can pass into the cervical canal and feels soft masses more or less easily removed with the finger.

It is naturally plain that the course of the microscopical examination would vary according to the nature of a case. If an ulcer, suspicious because of its clinical course, be found in the cervix, a test excision from the suspected area should be made for diagnostic purposes. It is better to choose a part which shows a transition from the ulcerating surface to apparently healthy tissue. It is urgently advised not to excise too small a piece, and for that reason it is better to use forceps and a knife than the curved scissors, with which, as a rule, small superficial pieces are removed. The wound should always be closed by deep sutures; and I advise that this step should not be an ambulatory one, since even with greatest care a severe hemorrhage may result if absolute quiet be not enjoined.

If the surface shows no changes pieces of the tumor must be removed with a sharp spoon, after having first attempted to obtain material for examination from the cervical canal with the finger. The curetting should not be done blindly, but after introduction of the speculum and fixation of the uterus with the volsellum. The material obtained must be prepared as described in the first part. I advise, when making such important examinations, the embedding in celloidin, so that many and good sections may be made, and that a portion of the specimen be cut with the freezing microtome according to the method of Pick or Benda.

Although I suppose that the general appearance of a carcinoma is known, I desire to discuss in a few words the accepted definition of the same. We understand by carcinoma a *tumor or neoplasm of epithelial elements in a connective-tissue matrix.* The epithelial elements lie in this groundwork in larger or smaller groups and form the so-called "carcinomatous alveoli" or "cancer nests." Even though this is a fairly exact description of the anatomical form, it alone does not suffice to make this weighty diagnosis, for we have repeatedly seen in our previous discussions that such epithelial nests may occur in a tissue without cancer being present. I call attention to the pictures we find in pointed condylomata, and to the hypertrophies of epithelium, and to the "illusion pictures" resulting from the plane in which the sections are cut. There

belongs, therefore, to a definition of cancer something else, and something equally important. This is the *relation of the growth* to the tissue which it penetrates. A carcinoma does not displace the other tissue structures, but *advances irregularly and is atypical in form, and is not stopped by other tissues. It destroys the gland borders and the vessel walls, and penetrates into the muscular tissue until finally nothing is left of the original tissues.* The latter does not remain without reaction; it reacts to the invading neoplasm, in the early stages, with a small-celled infiltration, more marked, perhaps, than occurs in *any other affection* in the cervix.

Before I pass to the microscopical condition in cancer of the cervix, I would discuss in a few words the so-called "carcinoma alveoli." In general it is said that the cancer alveoli are made up of epithelial cells. In my opinion this definition is not sufficient, for the beginner easily gains false views as to the appearance of these alveoli. He must know that these cells *do not possess the same regularity in size and position found in the case of cells forming normal epithelial tissue.*

FIGURE 19.—CELLS OF A CARCINOMATOUS ALVEOLUS WITH SO-CALLED "PROTOZOAL" CONTENTS.

What is really striking is the *irregularity* in the size and form of the cells. From small cells, of the size of the white corpuscles, all stages are found up to the largest cell forms. The nuclei are, as a rule, larger than normal nuclei of squamous epithelium, and the cell body surrounds the nucleus sometimes with less, sometimes with more protoplasm.

The nucleus shows great differences in form. In addition to simple nuclei there are often found in one cell two, three, or more nuclei, *i.e.*, numerous nuclear fragments.

If the specimens are properly fixed there is frequently seen a decided segmentation of the nucleus, to which recently special attention has been called by several authorities. There may be observed so-called "cell—*i.e.*, nuclear—inclusions," which are considered by some investigators to be protozoa. In Fig. 19 I have drawn such cells. It may be seen from this illustration how the carcinoma cells may differ in size. This is shown still more clearly by Fig. 20, in which a cancer alveolus is seen strongly magnified.

Here may be seen the absence of such regularity in the arrangement of the cells as is usually found in normal epithelial tissue. It may be seen that there is a confusion of large, larger, and smaller cells, between which are a few capillaries, a condition not occurring in normal epithelium. It is also noticeable that the cells do not always lie side by side, as in Fig. 20, but that very often leucocytes are found between these cells (Fig. 21).

After this description, we may define carcinoma as follows: Car-

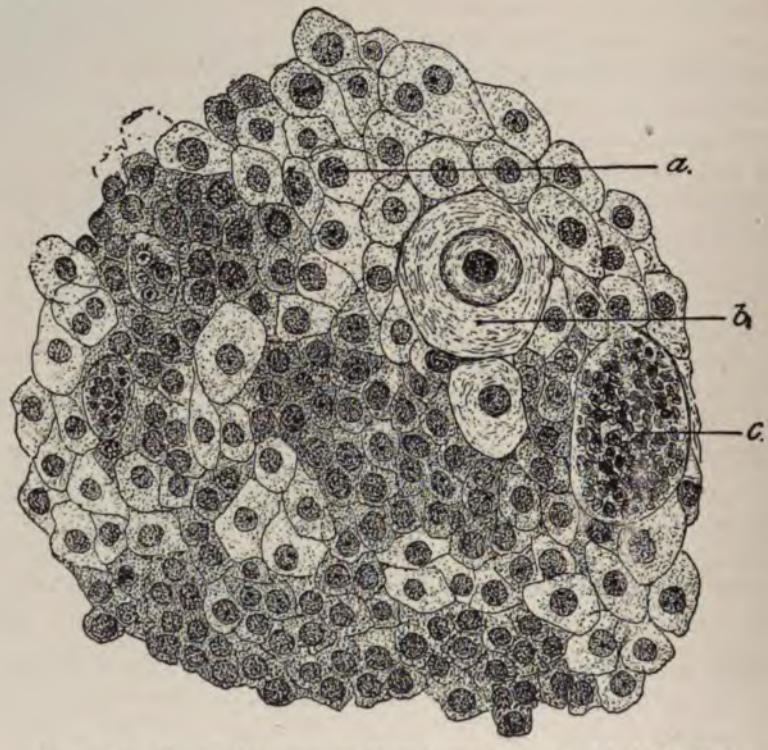


FIGURE 20.—CANCER ALVEOLUS BY HIGH-POWER LENS *(fixed in bichloride)*.

a, mononuclear cells; *b*, very large cells with bubble-like cell contents; *c*, capillary filled with blood.

cinoma is a neoplasm which consists of a tissue groundwork, more or less rich in cells, in which groups of various large epithelial cells are lodged. The latter form cords and penetrate the tissue, which they enter *irregularly and in every direction*. These cords are sometimes formed of a few cells, and sometimes of large masses. They break through other tissue layers and tissue forms, whose boundaries are destroyed by the epithelial cells entering them. They increase in this way until finally nothing is left of the original tissues. A carcinoma finds no limit at the muscular layer, breaks through the vessel walls, and de-

stroys the gland boundaries; in a word, it does not remain confined *to any one tissue,* but grows without limitation through various tissues.

These are the essential points, in my opinion, in making a diagnosis of carcinoma, whether it occur in the uterus or in any other portion of the human body. If these are established we may be certain that we shall not confuse a carcinoma with a benign epithelial hyperplasia or with an "illusion picture." In the latter cases the uniformity of the change, the regular arrangement of the elements, will always furnish the correct evidence as to the character of the change. Attention must be again called to the fact that the growth of epithelium within the gland lumina *is in no wise a justification for the diagnosis of a beginning carcinoma so long as the boundaries of the glands are not affected by the epithelia.*

FIGURE 21.—CARCINOMA OF THE VAGINAL PORTION OF THE UTERUS *(explanation in text).*

What the very beginning is we do not yet know; we shall no doubt learn even this when we learn the cause of carcinoma. Until then we must hold to the complete picture of a carcinoma, as we have given it above, in making a diagnosis.

These facts will be made use of in judging a test excision from the vaginal portion, the microscopical picture of which is to be found in the above illustration (Fig. 21). The section is so chosen that we see the transition from squamous epithelium to the affected tissue.

On the right side of the figure is seen the squamous epithelium *(a)* which forms the normal surface. This squamous epithelium shows already a deviation from its usual quality. As may be seen in the larger sections, in which more tissue can be observed, the squamous epithelium

becomes decidedly thicker in the direction of the carcinoma. The same is true in this section. In place of relatively few layers, as mentioned in the discussion of the normal condition, the squamous epithelium is seen to sink considerably into the underlying stroma. The nearer we go to the small-celled infiltration the more do the limits of the epithelial cells disappear, and it may be observed, above and to the left, that numerous leucocytes are forcing their way between the individual epithelial cells. Whether the spaces *(b)* are artificially caused by cutting or whether a pathological process is present cannot be stated with certainty. Near the squamous epithelium is found a tissue which shows a very marked small-celled infiltration. The same extends to the surface

FIGURE 22.—CARCINOMA OF THE CERVIX *(general view)*.
a, carcinoma alveoli; *b*, interstitial tissue.

as evidence of the presence of an ulcer. In this tissue are seen two large groups of lighter cells *(c)*, between which are found darker-stained round structures. The larger cell groups are composed of cells of various forms; those on the periphery are, as a rule, smaller than those situated centrally. We are dealing here with two large typical cancer alveoli. If we examine the areas infiltrated with small cells more closely we find at various points *(d, d_1, d_2,)* again isolated groups of cells which are sharply marked off from the small-celled infiltration; these are smaller cancer nests. It may be seen, therefore, that the entire tissue is quite changed in character. Of the normal constituents of the cervical

tissue none is present in the section, and we need not hesitate to diagnose a carcinoma with certainty from such a picture alone. If we study the specimen further (though this cannot be illustrated in a drawing) we find that such cell nests infiltrate the remaining cervical tissue, and that the small-celled infiltration extends still further into the deeply situated parts. In this specimen nothing can be seen of the connective-tissue groundwork, since everything is covered by the enormous small-celled infiltration. This is, however, as already mentioned, characteristic of the reaction of tissue to a neoplasm in the early stages. If the process had existed a longer time we should have found more fibrous connective

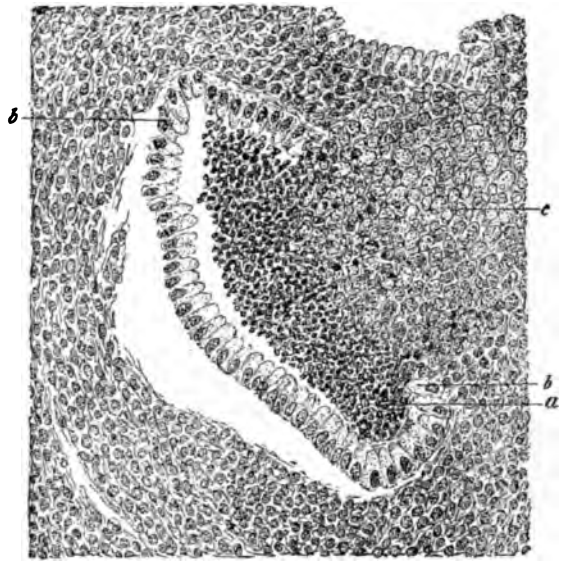


FIGURE 23.—GLAND WHOSE WALL AT ONE SIDE IS DESTROYED BY CARCINOMATOUS CHANGES.
a, dark round structures; *b*, normal epithelia which have retracted from the surrounding tissue; *c*, carcinoma which has, on the right, *broken through* the wall.

tissue in place of the exclusive small-celled infiltration. Such typical pictures of carcinoma are already well known from the text books on general pathology. Therefore I have given in Fig. 21 a view rarely seen in schematic drawings, but one which is often met with in microscopical sections. Fig. 22 serves as a general view with a lower power.

It shows by low power how the cervix is for the most part destroyed by the neoplasm; perhaps the connective-tissue groundwork may be considered the remains of the stroma of the vaginal portion of the cervix.

In the same way a carcinoma originating in the cervical canal is to be judged. The same characteristics are necessary in making a diagnosis, for the presence of glands in this part does not change this feature. As a rule the glands are increased in number in carcinoma without many

changes in them being evident. Sometimes it is seen that the gland walls are lined by a stratified layer of cylindrical epithelium. This alone, as we have often remarked, *is not sufficient ground for the diagnosis "carcinoma" if the other requisites be not fulfilled.* One of the most important of these requisites in the case of glands is *the destruction of the gland borders.*

If we find a picture like Fig. 23, no further proof is necessary of the destructive character of the process, for it is seen that one side of the gland is entirely destroyed by the entering neoplasm. Boundless growth through various tissues we have already given as an important evidence of the malignancy of a neoplasm.

3. Malignant Adenoma of the Cervix (Adenoma Destruens).

If firm cancerous prolongations are not formed and only the glands are found to be increased to an enormous extent, destroying all the interstitial tissue, the malignancy of this process (adenoma) will only then be microscopically proven on observing *the relation of these glands to the muscular tissue.* If the latter is also destroyed by these glands there is no doubt as to the diagnosis. If the growth of glands is, however, confined to the mucous membrane, *although the glands may be exceedingly numerous, the process is not necessarily malignant.* Only when the glandular type is no longer preserved, and when cords of atypically arranged cylindrical cells substitute the original tissue, are we justified in making the diagnosis of a destructive adenomatous neoplasm. I should not like to make any fast rules to govern the beginner in such a case, since the diagnosis of this affection requires great practice, and even the experienced pathologist often finds difficulty in properly construing such specimens, especially if he is furnished with only curetted particles and not the entire organ. The coexisting clinical condition and symptoms are of great weight, and often everything must be fully considered in deciding the practical management of such a case. Under pathology of the endometrium we will consider these relations more fully. In the cervix the occurrence of a pure malignant adenoma without carcinoma is rare. In the course of the last few years a few such cases have been reported. Rather more frequently combinations of adenoma and carcinoma (adenocarcinoma) come under observation.

4. Sarcoma of the Cervix.

Sarcomata occurring in the cervix are always circumscribed tumors, whether they are pedunculated (the polypoid form) or whether they grow far into the muscle. Macroscopically a sarcoma may look like a carcinoma, especially like that form called a "cauliflower growth." A decision as to whether it is a carcinoma or sarcoma requires a microscopical examination.

Sarcoma, as is known, originates from the cells of the connective tissue and is made up of closely arranged, round or spindle cells. A complete separation of these two forms can usually not be made. Giant cells are also found. A fine connective-tissue net lies between the cells. It shows at times a strong edematous infiltration or else a myxomatous degeneration. Thus the individual papillary formations are swollen, and from these results the cauliflower-like growth, so that the entire tumor has a racemose appearance (sarcoma botryoides). In the harder central parts of this neoplasm and in its base are found normal areas of connective tissue rich in blood, and nests or strands of sarcoma cells, while the peripheral parts resemble young connective tissue or mucous tissue. If the surface is not ulcerated it is usually covered with one or more layers of cylindrical or squamous epithelium, depending on whether the tumor originates from the mucous membrane of the cervix or of the vaginal portion (Pfannenstiel, Pick). Between the sarcoma cells remains of the cervical glands may be found.

The Origin of Sarcomata of the Cervix.

The sarcomata of the cervix, as is the case in other organs, may originate from the various elements present in the matrix. They arise:

(α) From the Upper Layers of the Mucous Membrane.

and then form especially grape-like tumors. These, as a rule, are rare; they may reach a considerable size and grow entirely outside of the vagina. The occurrence of such tumors is observed in adults and also in children. At times there develops, in a carcinoma, an adenoma out of the remaining epithelium of the cervical mucous membrane, *i.e.*, the glands, so that a mixed tumor results *(adenosarcoma)*. If the connective tissue is myxomatously degenerated there results an *adenomyxosarcoma.* If, in addition to the glandular formation, cystic structures also are found, we speak of a *cystic adenosarcoma.* From an adenosarcoma there may easily result a transition into carcinoma, so that a form of growth is seen which is known as a *sarcomatous adenocarcinoma.*

A second form of sarcoma results

(β) Through Sarcomatous Degeneration of a Cervical Myoma or Fibroma.

In this case the sarcoma cells are said to result from a direct transformation (metaplasia) of the myoma cells, or from the connective tissue between the muscle bundles. In most of these cases we are concerned with a pure spindle-celled sarcoma.

Another special form of sarcoma is:

(γ) Lymphatic Endothelioma.

The histological picture of this form of sarcoma is almost identical with that of an adenocarcinoma, and is only to be distinguished from

it through its different origin. It is to be mentioned that, according to the views of several authors, the endothelium of the lymph and blood vessels is of entodermal origin (?). Then it must be considered epithelium, and the tumors resulting therefrom can therefore not be considered as belonging to the group of sarcomata.

5. Myomata, Fibromata, Fibromyomata.

More rarely than in the body of the uterus, there are found in the cervix benign connective-tissue neoplasms. These are situated either under the mucous membrane or may by further growth bcome pedunculated (polyps). They then fill the vagina and protrude from it; or there result enlargements, especially of the posterior cervical wall, which at times may fill the entire true pelvis. Rarely are we concerned in these tumors with histologically pure myomata or fibromata, but generally with fibromyomata, which contain muscle bundles between fibrous connective tissue.

At times glandular and cystic deposits are found, as is the case in myomata of the body of the uterus *(cystadenofibroma* of the cervix).

As mentioned above, there may occur in these a sarcomatous degeneration (myosarcoma) and, as a rule, polypoid formations. There has been described, in addition to the smooth muscle fibres, the presence of striated muscle fibres *(leio- and rhabdomyosarcoma)*. (See Part III.)

6. Tuberculosis of the Cervix.

Primary tuberculosis of the cervix occurs infrequently, but I believe that with careful microscopical examination more cases will be found, since recently attention has been frequently called to its occurrence. I myself have had several striking cases which were of interest in various ways. The clinical symptoms and the appearance shown by the speculum were very much like those in carcinoma. There were profuse irregular bleedings, great discharge, and an ulcerated appearance of the cervix. Proof of the real nature of the affection is given only by the microscopical examination, which I carried out in my case because I suspected it of being carcinoma. The following picture (Fig. 24) shows that the surface is covered by nearly normal squamous epithelium *(a)*. On the left side of the figure are seen the typical spaces lined with cylindrical epithelium, which we have learned to know in the case of the so-called "erosions." On the right side, on the other hand, are seen in the stroma several characteristic tubercles *(c)* with giant cells *(d)*. The stroma is infiltrated with small cells in places, but shows no decided changes of any other kind.

In a second case there was decided hyperplasia of the epithelial cells of the cervical glands, so that the glands were lined with several layers of cylindrical epithellum in the stage of proliferation. If we consider

that in tuberculosis there may occur a growth of the squamous epithelium (Carl Friedländer's atypical epithelial growth) with the formation of reticular strands in the subepithelial tissue, and if we reflect, on the other hand, that in carcinoma giant cells have also been described, it is evident that in striving for a very early microscopical diagnosis errors may easily occur. I am convinced that the uterus is frequently removed for "beginning carcinoma" where in fact *tuberculosis is present,* and in the future more attention must be paid to this point. The presence of tubercle bacilli, of so great importance in the differential diagnosis, is not, as a rule, demonstrated by the examination of test excisions.

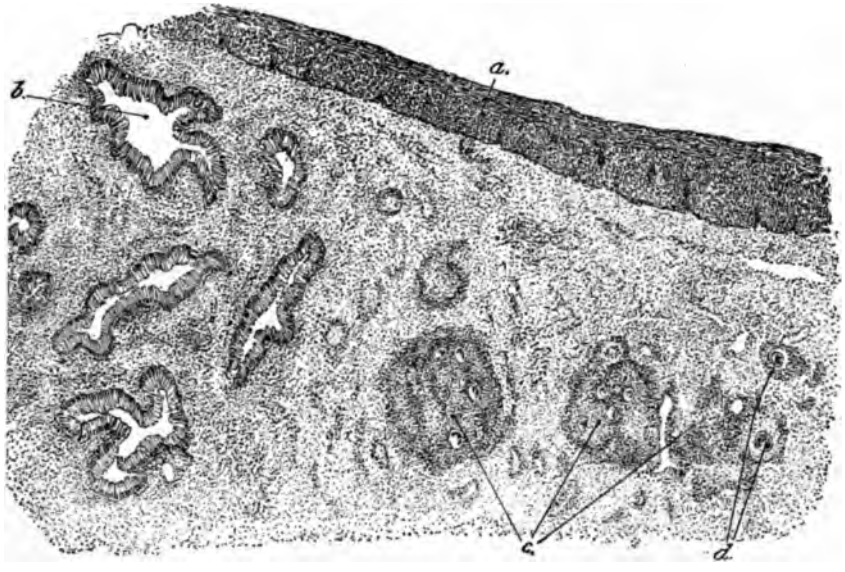


FIGURE 24.—TUBERCULOSIS OF THE CERVIX.

a, squamous epithelium; *b*, glands; c, tubercles with giant cells *(d)*.

IV. THE UTERUS.

The body of the uterus is that portion which begins at the internal os and extends to the fundus. It is composed of mucous membrane, of muscle, and of a peritoneal covering. The portion of chief interest is the mucous membrane, or endometrium, since by far the largest proportion of uterine affections originates therein, and, on the other hand, it is usually affected in most of the other pathological conditions of the internal genitalia. Since, further, the curettings of the uterus for diagnostic or therapeutic purposes consist almost always of only mucous membrane, it is of great importance that we become intimately acquainted with its normal appearance. It is more important here than in the cervix to recognize its normal composition, for there is no other tissue in the human body which, in its normal condition, is as liable to varia-

tions as the uterine mucosa. It is just as different at puberty and in advanced age as during and after menstruation, and as during and after pregnancy until the restoration to its original condition.

It is very easy for those who do not know these conditions to consider normal appearances as pathological. We will therefore discuss the varying normal relations before passing on to the study of its pathological investigations.

A. THE MUCOUS MEMBRANE OF THE UTERUS (ENDOMETRIUM).

1. NORMAL ANATOMY.

The mucous lining of the uterus lines the muscle wall which forms the hollow body of that organ. Externally the latter is bounded by a peritoneal covering. Under this, and so firmly united to it that it cannot easily be removed, lies a thin longitudinal muscle layer, which is followed then by a layer of richly developed elastic connective tissue. In this are found the blood vessels which supply the body of the uterus, and the branches which pass to the muscle bundles and to the mucous membrane, in which they end as a network of capillaries. The vessels running circularly are of considerable size. The arteries are remarkable for the thickness of their walls.

The muscular layer which follows this vascular layer forms nearly the entire thickness of the uterine wall. It consists, according to the statements of certain text books, of an external longitudinal layer, of a layer of interlacing fibres, and of an internal circular layer whose fibres extend into the lowest layers of the mucous membrane. According to recent examination, such a schematic division cannot be countenanced. According to the sections which I have made, it appears that the main mass of the uterine muscle is formed by a circular layer, in which fibres running in other directions are present. Immediately under the mucous membrane a thin longitudinal layer of muscle fibres can be distinguished. The mucous membrane possesses no submucosa (Fig. 4). The thickest layer of the muscle has been called muscularis mucosæ, and, correspondingly, the vascular layer has been called the real muscle. This view, however, stands quite alone, and has been rejected as unstable by recent investigations.

(α) The Endometrium after Puberty, in a State of Rest (i.e., between Two Menstruations).

The endometrium lines the inner surface of the uterus in a layer one to two mm. thick. It is grayish, faintly shining, and of soft consistence. It consists of a stroma in which vessels run, and of the uterine glands.

The stroma, *i.e.*, the interglandular tissue, may be called "lymphoid

tissue." It consists mainly of rounded oval cells, of almost the size of white blood corpuscles, which lie in a very fine connective-tissue reticulum, which in comparison with the cells stands quite in the background.

The cells are not always oval, for around the glands and in the region of the muscular tissue there are some which are spindle-shaped. The cell boundaries themselves are recognized with difficulty in the specimens hardened in alcohol, for the nucleus occupies the greater part of the cells, and its membrane and transparent protoplasm lie so near the external limit of the cell that usually only this nucleus is seen.

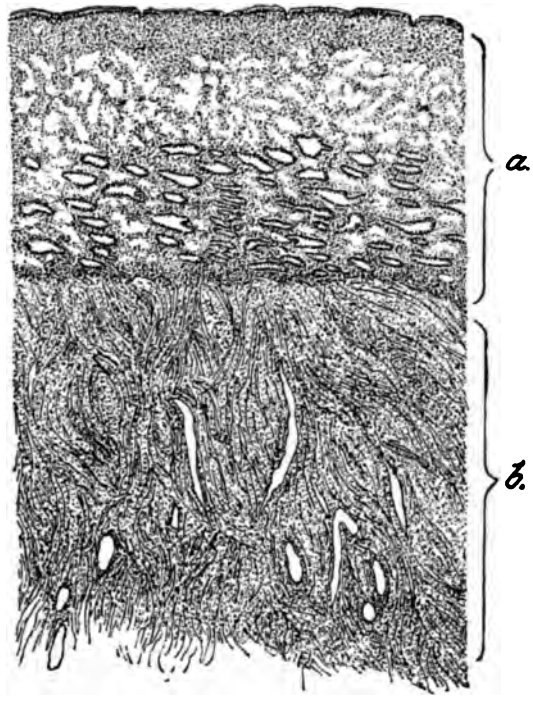


FIGURE 25.

a, almost normal endometrium (slight increase in glands); *b*, muscle—the boundary between muscle and mucous membrane is in this specimen very distinct. The surface is covered with cylindrical epithelium. The epithelia in the glands near the surface have fallen out. Gland openings do not appear in this section.

On its inner surface, *i.e.*, toward the cavity, the mucous membrane is covered with simple *ciliated* cylindrical epithelium. The mucous membrane is not sharply marked off from the muscle, for a gradual interweaving of mucous membrane and muscle fibres occurs. We find, therefore, muscle fibres in the deepest layer of the mucous membrane, and, *vice versa*, mucous membrane elements in the superficial muscle layers.

The surface epithelium, whose cells are somewhat lower and broader

than those in the cervical canal, does not run uninterruptedly over the surface, but forms, at certain intervals, funnel-shaped depressions, which appear through a lens like punctate openings. These lead into the uterine glands, which are lined with the same epithelium as that found on the surface.

The uterine glands are tubular glands which perforate the entire mucous membrane perpendicularly or obliquely, so that the fundus of these glands frequently lies in the superficial layers of the

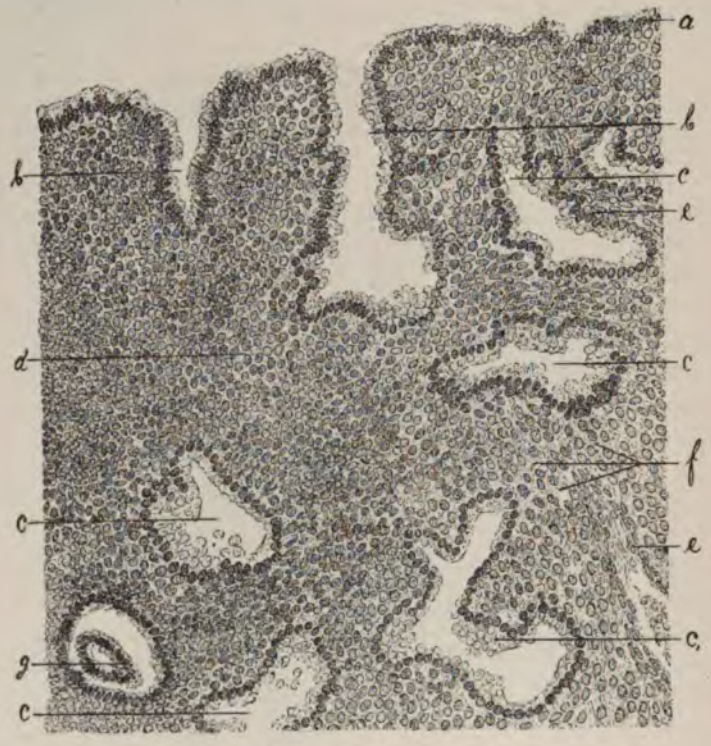


FIGURE 26.—ALMOST NORMAL ENDOMETRIUM *(highly magnified)*.

a, surface epithelium; *b*, longitudinal section through gland; *c*, transverse and oblique sections of glands; *d*, interstitial tissue consisting mainly of oval nuclei (cell borders not evident); at *e* they are spindle-shaped; at *f* a little more fibrous tissue is present between the cells than elsewhere; *g*, invaginated gland.

muscle wall. In their upper third the glands, as a rule, follow a straight course, while deeper they are often twisting and sometimes forked. In this way it happens that in sections perpendicular to the surface there are found in the upper layers glands in longitudinal section, while in the deeper layers they are seen transversely or obliquely cut.

In such a microscopical picture are seen spaces lined with epithelium, some long spaces, others oval or circular. Since the glands often divide

deeper down and take a twisting course, we naturally find the gland lumina cut through more frequently there than where the glands run straight without dividing. In this way the impression may be given that a pathological increase of glands is present. A criterion in judging this condition is the number of glands in the upper layers, when seen by a lens of moderate power.

The width of the gland lumen is variable; a definite normal size cannot be expressed in figures. Frequently the lumen is so narrow that the epithelial cells of the opposing sides are in contact, so that the canal is narrowed. Still, a rather wide gland cannot be considered pathological. At times the form is not symmetrically round, but, as in the case of the cervical glands, the interstitial tissue rises in places toward the lumen of the gland, so that an irregular form results, as well as a narrowing of the lumen. Not infrequently there is found in a gland lumen a second circle of epithelial cells, an evidence of invagination of the gland wall (Fig. 26, *g*).

Attention is called to another condition. Very frequently the glands are separated from the interstitial tissue by an empty space which surrounds the gland wall in part or entirely like a crescent. This is caused by the varying action of alcohol on the stroma and the epithelium. The contraction of the epithelium is usually very even, and the contracted circle of cylindrical epithelium is so sharply outlined that from this fact alone the presence of a membrana propria may be taken for granted. In this way the glands are sharply defined from the other tissue. Another fact speaks for the presence of such a membrane. If a thin section be brushed in water the epithelial cells fall out, and there remain in the connective tissue only well-defined spaces, whose endothelial-like boundary can be recognized as a separate membrane. Quite different from these spaces, which normally are not present, are the falciform cavities or spaces which now and then separate a gland wall from the connective tissue. These are sections of capillary vessels, as a high-power lens shows the presence of an endothelial capillary wall.

We now come to the discussion of the VESSEL DISTRIBUTION in the endometrium.

The vessels, arteries, and veins, running in the muscle, branch more and more as they approach the mucous membrane, and form a capillary network in the latter layer. In only those parts lying near the muscle do we see in the mucous membrane isolated small arteries and veins. In the inner layers, on the contrary, only capillaries are present, whose blood surrounds the glands and flows through the other tissues. The number of venous capillaries is said to be far surpassed by the number of arterial capillaries. Since these are very narrow and thin they appear indistinct except in injected specimens. There is often only a very fine space between two cells, which gives the impression that a cell is missing. Only through the presence of endothelia (by strong magnifica-

tion) and the use of thin sections is it proven that in fact we are really dealing with capillaries.

In addition to the blood vessels the endometrium possesses an extensive network of lymphatics, concerning whose microscopical appearance there are as yet no reliable descriptions. It is generally said that the uterine mucous membrane, from the vaginal portion of the cervix to the fundus, is permeated in all directions by a lymphatic network with the very finest ramifications. How these look, whether they have walls of their own (which seems probable, according to the latest observations), or whether they are only tissue spaces, or whether they differ much from blood capillaries, or whether they contain valves and form dilatations or sinuses—all these are questions as yet unanswered, but of the greatest importance to normal and pathological anatomy.

(β) The Endometrium during Menstruation.

Regular menstruation, recurring every four weeks, which is to be considered as a discharge of blood from the uterine cavity, causes defined and regularly recurring changes in the mucous lining of the uterus. These depend in a great measure upon the blood vessels.

In the normal endometrium, as has been said, we find great difficulty in demonstrating the capillaries. During menstruation, however, these are congested with blood, and frequently to such an extent that they may dilate to a very great size.

Since the vessels do not open on the inner surface of the uterus, no outward bleeding can occur so long as they are only turgid. Such external bleeding occurs only when the pressure is so great that a part of the blood is pressed out of the vessel channels and is poured out into the tissue. This occurs, in fact, in every menstruation. We find then in the interglandular tissue larger and smaller areas of free blood, which is also poured out between the meshes of the interglandular tissue, either pushing it aside or destroying it. The latter fact, doubted by many writers, may be recognized by finding inside of these blood extravasations cells of the original mucous membrane tissue, partly preserved and partly degenerating.

This blood, which is now no longer in its usual channels, trickles, under the constant pressure of the continually following outflow, wherever it meets with the least resistance. It passes between the epithelial cells and into the glands, completely filling them, or it flows directly through the surface epithelial layer into the uterine cavity, and from here is expelled by *contractions of the uterus.*

This forcible penetration of the blood through the epithelial layer of the glands and of the surface causes, as may be readily understood, a shedding of epithelial cells. *This shedding, however, never reaches such a degree that the surface is completely denuded of cells; only in isolated areas are these thrown off*, and are found in the examination of

the menstrual fluid among the red blood cells. That in this way the superficial layers of tissue may also sometimes be thrown out, especially the areas loosened by blood, deserves no further mention.

In addition to red blood cells, white blood cells also naturally make their exit from the vessels. They lie in larger or smaller groups in the tissue, and are easily mistaken for areas of small-celled infiltration, without in reality an inflammatory condition being present. The cells of the interstitial tissue retain, as a rule, their original form, but some may be destroyed by pressure and others may undergo fatty degeneration. No other changes are to be found during menstruation in a uterine membrane previously normal.

It is the same with the epithelial cells. In spite of the great hyperemia they do not proliferate, perhaps because the hyperemia as a rule disappears in a few days. On the other hand, changes from the normal, as a result of the great mechanical pressure, are also observed in these. We find many epithelial cells loosened from their points of attachment. They pass directly from the surface into the menstrual blood, or else fill the gland lumina and are then passed on into the uterine cavity through the excretory ducts.

To recapitulate, the changes which are caused by menstruation, in the normal mucous membrane, are almost exclusively of a mechanical nature, consisting of a destruction of some cells of the interstitial tissue and of the epithelium through pressure of the extruded blood. In part there is also a fatty degeneration of the cells.

As is known, the uterine mucous membrane possesses a remarkable power of regeneration, and there occurs, very soon after the cessation of menstruation, a restitution, so complete that only a few days later no remains of the previous changes are found. The detached epithelium is replaced by the remaining epithelial cells, and the blood poured out into the tissue, which has not reached the uterine cavity, is resorbed together with the interstitial tissue cells which have begun to degenerate.

In discussing these normal menstrual changes we must consider an anomaly of menstruation which does not infrequently come to our notice, and which is of great diagnostic interest. It is that form of menstruation in which expulsion not only of fluid blood, but of entire layers of mucous membrane, or even the entire mucous lining of the uterus, occurs. Since the extrusion of such a membrane is accompanied by severe pain, this anomaly has been given the unfortunate name *dysmenorrhea membranacea,* thus classifying the anatomical product *tiva* which is found in recent works. This name is incorrect because does not agree with anatomical facts, is the name *endometritis exfoliativa* which is found in recent works. This name is incorrect because it this is not an *inflammatory* change. Indeed, the expulsion of such a membrane may occur in a uterine lining previously inflamed without this being the result of inflammation; for this anomaly occurs in mucous

membranes which show no sign of inflammatory changes, just as in intra- or extrauterine pregnancy the expulsion of the decidua is no more to be considered the result of an inflammation than the above condition during menstruation. It is a process whose cause we do not yet know. We must, therefore, be content with the existing fact, and it seems to me better to call the membrane expelled during menstruation

Decidua Menstrualis.

By this name the macroscopical appearance of this membrane is also described.

We have seen that in ordinary menstruation, at times, in addition to the epithelia, individual shreds of the mucous membrane of the uterus are expelled. The menstrual decidua is then a cast of the entire interior of the uterus, which is thrown off complete or in pieces. What is the microscopical composition of such a decidua?

In my opinion it would be false to establish a special type, and to make certain cells of the interstitial tissue or changes in the epithelia characteristic of such a decidua. One thing only may be said with certainty, and that is that this membrane consists of the *superficial layers* of the uterine mucous membrane. Accordingly, it will be found to contain the various elements of this lining, namely, glands, epithelium, interglandular tissue, and vessels. Whether these elements reflect the picture which we have learned in viewing the normal mucous lining, or whether changes of an inflammatory kind are present, depends upon the state of the mucous membrane before the menstruation. I believe that in this way the various views of the different authors may easily be brought into harmony, for one considers this and the other that cell form of the interglandular tissue, and still another this or that change of the gland or superficial epithelium, to be characteristic of this condition. The following figure (Fig. 27) represents the microscopical picture of such an expelled menstrual decidua, whose mucous membrane must previously have been of normal character. The interstitial tissue shows the well-known oval cells which we have already learned to be the normal constituents of the interglandular tissue. The abnormal element is the infiltration with small round cells; but this is natural, since we are dealing with a menstruating mucous membrane into which red and white blood cells have entered from the vessels. That these round cells lying isolated between the cells of the interstitial tissue have really come from the vessels is evidenced by the marked grouping of such cells about the vessels themselves. A third essential constituent is found in the section through a gland at *d*. This does not show the normal round form, but is somewhat dilated, which must not be considered pathological, since the uterine glands possess, as a rule, no defined mathematical form, but have sometimes a narrower, sometimes a wider lumen. The epithelia of the glands are not much changed from the

normal, even though they are closer together than usual. A specially characteristic change, such as a decidua shows in pregnancy, is, however, not present. Inside, the gland shows an indistinct mass which seems to be a clot (mucus, blood). This corresponds to the ordinary occurrence in menstruation. That the capillaries found in such casts are turgid with blood deserves no special consideration.

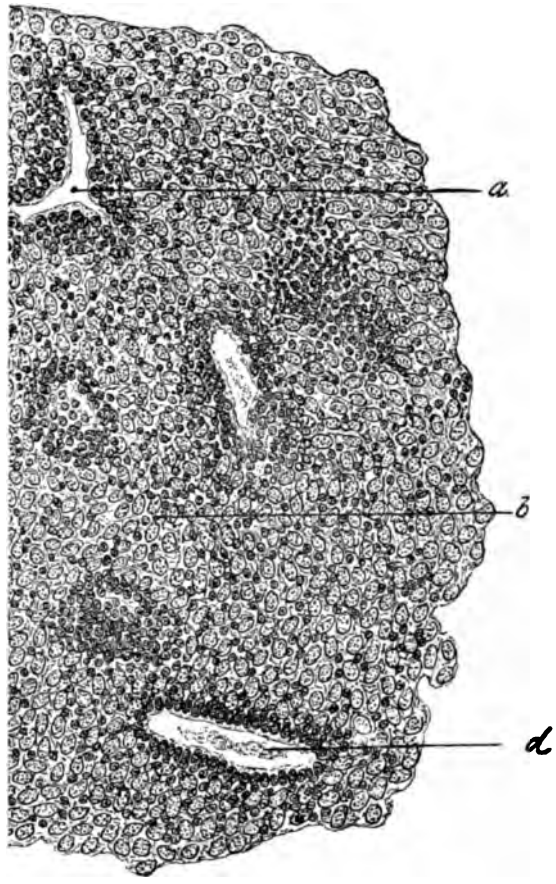


FIGURE 27.—MENSTRUAL DECIDUA.

a, section through vessels surrounded by groups of round cells; *b*, interglandular tissue consisting of normal cells with scattered round cells; *d*, section of a gland somewhat dilated—its epithelia are somewhat smaller than normal.

In the above section there are, therefore, all the constituents of the mucous membrane in an almost normal condition. If an inflammation with productive changes had previously existed, then all the cells could take on those forms which we shall later recognize in discussing inflammatory processes. They can develop into large decidua-like cells or show regressive changes. At any rate, it would be false to say that the large cells of the interstitial tissue resembling those occurring during pregnancy are characteristic of a decidua shed during menstruation;

just as false as if an accidental increase of connective tissue were considered typical. If, on the other hand, productive changes in the gland epithelium had been present—for instance, proliferation which led to the formation of several layers—the same condition would be found in the mucous lining expelled during menstruation.

Since the shedding of such a menstrual decidua is often accompanied by profuse bleeding, the question for the medical man is, whether or not an abortion is in progress—a question whose decision might be of great importance in a court of law.

Is it possible, with the aid of a microscope, to decide *whether such an expelled uterine cast or piece of tissue is related to a pregnancy or not?*

For this purpose we must consider those changes to which the uterine lining is subjected during pregnancy. As pregnancy is a physiological function of the uterus, the discussion of the changes occurring therein belongs naturally to the normal anatomy of the uterine mucous membrane, just as is the case with menstruation. Of course, the change in the uterine lining in pregnancy is so decided—certain elements which we have learned above disappear entirely and others are newly formed, while the form of still other elements is changed—that it is always difficult to explain to the beginner that all these changes lie within physiological limits. At any rate, the microscopic pictures bear such a resemblance to pathological processes, at least in small pieces removed for diagnostic purposes, that even the practised microscopist may diagnose from such a specimen a malignant neoplasm, may extirpate the uterus and subsequently find a normal pregnancy without the least evidence of a pathological process.

In the present discussion we are concerned exclusively with practical and weighty questions, and not with special anatomical examinations. Diagnostic doubts exist only in the early months of pregnancy, when the enlargement of the uterus is still slight. If, for instance, as often occurs, the fetus is expelled unnoticed, and if subsequent bleedings of an irregular type result, which bleedings in a short time weaken the patient, or if we are dealing with an expelled piece such as occurs in extrauterine pregnancy, then these evidences are often of such a character that a suspicion of the existence of a neoplasm may seem justifiable. The history, which should be an important factor in diagnosticating a pregnancy, cannot be considered decisive in this case, for it is known that all possible deviations from the normal occur. Naturally, in doubtful cases, it would be of great value if microscopical examination could decide with certainty whether we are concerned with a pregnancy or a neoplasm. Frequently it depends upon this diagnosis whether an operation, and what sort of an operation, should be done.

(γ) The Endometrium during the First Months of Intrauterine Pregnancy.

On the occurrence of pregnancy a very peculiar stimulation is ex-

erted upon the uterine mucous membrane, whose product results in a mucous lining thickened to ten or more times its original depth. This thickening is caused by the growth of the various elements forming the mucous membrane, which are affected in varying ways by this event.

At the beginning of pregnancy, and hand in hand with the increase in thickness of the mucous membrane, an enlargement of the glands takes place. This is irregular in that the parts situated near the outlet are stretched and considerably widened, while the deeper parts of the glands, as far as the muscle layer, become very tortuous. In microscopical sections this varying increase is such that the inner parts of a section show less numerous glands, while those portions situated in the external layers of the mucous membrane and near the muscle show so many gland lumina that the interglandular tissue steps into the background. This initiates *a division into two layers,* which later becomes still more marked; for the more the interglandular tissue disappears in the external layer, where there remains only a honeycombed tissue *consisting almost entirely of glands,* the more does this interstitial tissue develop in the inner layer, so that here the very opposite occurs, namely, *a disappearance of the glands* as a result of a complete overgrowth of the interstitial tissue. In this way there occurs a division of the mucous membrane into two parts, which, in accordance with the appearance and consistence of the tissue, is called the "compact" or "cell layer" and the "spongy" or "glandular layer." The "cell layer" is that which is thrown off in the expulsion of the ovum, while the "gland layer" remains in the uterus and is intended to furnish the regenerating mucous membrane with epithelium for the glands and for the surface lining.

If these elements are viewed singly it appears that the epithelium lining the glands loses its form entirely (Fig. 28, *a*). In place of the delicate high cylindrical cells there are formed flat cubical structures which become flatter the longer pregnancy continues, so that they are broader than long, contain little protoplasm, and furnish cells almost entirely filled out by the nucleus. The resemblance to cylindrical cells almost disappears, but their resemblance to squamous epithelium is only an external appearance, as their origin is, as we have just seen, entirely different.

If we observe the various sections of glands in Fig. 28 it will be seen that these have quite a different form from that found in the normal endometrium. In comparison with this, the glands are here dilated and of irregular form. Nothing is seen of the almost circular section, in which the gland lumen represents only a small space surrounded by high epithelium. What, however, is striking in this figure is the triangular form in this case, although pregnancy had existed only about seven weeks. This triangular shape becomes continually more marked, and the

gland remnants, which at the end of pregnancy lie close to the muscularis, have, as a rule, only this form.

I have gone into these changes in the glands extensively because great importance has been attached to them in test curettings in making the diagnosis of pregnancy. It has been said that in such pieces, or in pieces spontaneously expelled, the flattening of the cylindrical epithe-

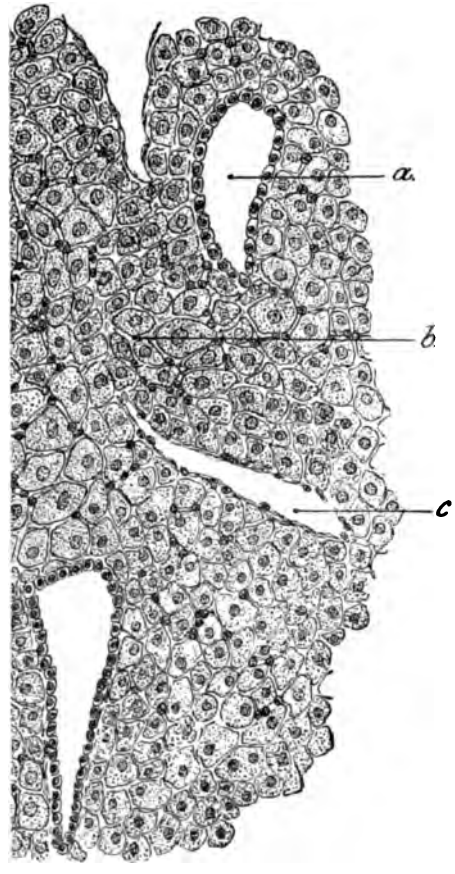


FIGURE 28.—DECIDUA IN INTRAUTERINE PREGNANCY *(abortion)* AT THE SECOND MONTH *(curetting)*.

a, section of a gland with flattened epithelia; *b*, interstitial tissue consisting of the so-called decidua cells, between which at certain points irregularly scattered round cells are seen; *c*, section of a vessel—in the wall are endothelia.

lium is a characteristic of pregnancy. Even though it must be granted that this change in the epithelium is very striking and very marked, and that the skilled microscopist, who continually has the opportunity of making such examinations, attaches without doubt, in judging such a specimen, great weight to the flattening, the diagnosis of pregnancy should never be made from that fact alone. Such uncertain statements

should not be taught the beginner. In this way disaster may easily result when we consider the importance of such diagnosis. Besides, we shall discuss further on the possibility of making the diagnosis "pregnancy" from the decidua cells alone.

It remains for me to discuss in a few words the change in the surface epithelium. This is subjected more than the glands and their epithelium to the pressure of the growing ovum. In consequence it becomes flattened earlier than the latter, and forms, after a short time, only an endothelial-like covering, which in the second half of pregnancy disappears, so that at that time the decidua comes into direct contact with the membranes, with which, as is known, the "cell layer" unites, being then thrown off with the ovum *in toto* at the end of pregnancy.

The same changes as those on the surface occur in the epithelium which lines the outlet of the glands, and in the glands in their entire course. Here, likewise, the epithelial cells are changed into a very fine endothelial-like layer, which later on disappears, so that it is no longer possible to say from the appearance of such a canal whether or not we are dealing with a gland. This can only be proved by following its course.

We are now to consider the interstitial tissue. This is still more changed than the glands and the epithelium. The cells of the interstitial tissue (Fig. 28, *b*) enlarge at the beginning of pregnancy, and increase in size the more pregnancy advances, so that at its end they are five to six times as large as those in the non-pregnant endometrium. This increase in size in the individual cells *concerns the protoplasm more than the nucleus;* for, while in the normal endometrium the nucleus forms the main portion of the entire cell, and the protoplasm is relatively small, the contrary is the case with the cells of the pregnant endometrium. The nucleus retains almost its original size, while the cell body continually grows, and in this way there results in these so-called "decidua" cells a certain resemblance to squamous epithelium. This resemblance becomes still greater through the continuous pressure exerted upon the tissue, and the cells lose their original oval form and become mutually flattened. In addition, under the continued growth of the cells, the tender connective-tissue network between them disappears, so that the large decidua cells lie almost in direct contact with each other, being separated only by small spaces in which here and there small round cells are visible. The whole presents a very uniform and regular picture, so sharply characterized that we would naturally believe any doubt with regard to the diagnosis of such a specimen excluded. When we are dealing with such normal conditions we are, as a rule, in a position to make a positive diagnosis.

In our practical examinations we are usually dealing, *not* with normal, but with pathological conditions; and although they have been described above, they are not present with the same clearness, but are

usually combined with other pathological changes, which permit of different possibilities in the way of diagnosis. The discussion of this question will be our task when describing the individual affections.

The *vessels* of the interglandular tissue take part decidedly in the changes of the other elements. Veins and arteries, so far as they run in the mucous membrane, lose their muscle wall during pregnancy, and present only simple endothelial channels which are not so delicate and thin as the capillaries of the normal endometrium, but take part in the general growth and form large spaces filled with blood. At the location of the placenta, *the decidua basalis,* or decidua serotina, these endothelial tubes open on the surface and send their endothelium upon it, since the epithelium of the former disappears; and they also send their endothelium over the chorionic villi (?), so that the spaces between the villi are walled off in their entire circumference from the fetal structures. They form, therefore, nothing but *dilated blood sinuses originating from the maternal decidua.*

These relations, the recognition of which has caused so many disputes, are, according to recent investigations, no longer to be doubted, and are confined only to the first weeks of pregnancy. Later the epi- or, better, the endothelium disappears here as upon the surface, and the maternal circulation comes into direct contact with the fetal elements.

It is to be hoped that these remarks suffice to show the changes of the endometrium during the early period of normal pregnancy. Even though an extrauterine pregnancy is not normal in the obstetrical sense, the changes which it causes in the mucous lining of the uterus cannot be considered pathological. They are nothing else than the changes of pregnancy—*i. e.,* only a variation of the endometrium, which is subject, as we have seen, to so many other variations in its normal structure.

(*A*) The Endometrium in Extrauterine Pregnancy.

All examiners are united in the opinion that in an extrauterine pregnancy a decidua is formed in the uterus, *i.e.,* a membrane which is later thrown off. Concerning the structure of this decidua, on the contrary, opinions are at variance, at least with regard to the membrane SPONTANEOUSLY expelled from the uterus—an event which does not always but which does frequently occur in extrauterine pregnancy. This spontaneous shedding is usually a sign that the fetus is dead. If we can determine by a microscopical examination that this decidua originates from an extrauterine gestation, it is without doubt of great value in determining the treatment. The changes which take place in the formation of a uterine decidua connected with an extrauterine pregnancy are the following:

The endometrium shows changes which are distinguished in two ways from those in intrauterine pregnancy. First, the stimulus is decidedly less when the ovum is not in the uterus; therefore the increased

conditions in the way of growth are not so decided as in normal pregnancy. Second, the formation of the decidua is completed at two to two and one-half months. Up to that time the entire uterus takes part in the growth, so that in palpation, if the entire ovum is not felt as an isolated tumor, a difference as regards the size of the uterus does not exist between an intra- and an extrauterine pregnancy. After this time, if this condition be interrupted in some way or other, the uterus undergoes involution; if, on the other hand, the pregnancy continues (the ovum can develop to full term outside of the uterus), then in spite of this fact the growth of the uterus ceases. As a rule, the uterine decidua undergoes involution in the latter months of extrauterine pregnancy. Under these general suppositions the change in the endometrium occurs in such a way that in the first three weeks almost the same conditions are to be found as in a normal pregnancy.

The cells of the interstitial tissue enlarge, but even in the third month *do not attain the size seen in these cells at the end of the first month of an intrauterine pregnancy.* The increase concerns mainly the cell body, while the nucleus remains about the same size as before. A further difference, as compared with normal pregnancy, is that *the cells do not become mutually flattened,* but retain almost their original oval form. This condition is to be explained by the different conditions of pressure which exist. In the second month—and here especially are the opinions of different authors at variance—the growth of the cells of the interglandular tissue is increased to such an extent that, as a result of my examinations, there occurs the formation of an exclusive "cell layer" as the inner lining of the mucous membrane. The gland openings, as in intrauterine pregnancy, are overgrown, and only the deeper part of the glands, the fundus, remains clothed with epithelium. There is formed then a continuous "cell layer." *This alone, in case of spontaneous expulsion of the decidua, is thrown out of the uterus, while the "gland layer" remains behind.* The epithelial cells of the glands are distinctly flattened. In the increase in thickness of the mucous membrane the glands become elongated near their openings, while toward the muscle layer they are tortuous. The superficial epithelium becomes flat, so that at completion of the decidua formation only a delicate endothelial-like covering is present. The following picture gives a microscopical section through such a membrane (Fig. 29).

I have had repeated opportunity to substantiate this condition in the case of membranes *spontaneously* expelled, and I must therefore consider it as usual. If in the early stages of an extrauterine gestation decidua is expelled, which is unusual, sections of glands may be found. The epithelial cells have the broad cubical shape characteristic of pregnancy. A positive diagnosis cannot be made from the examination of the microscopical specimen alone.

The depression which is seen in Fig. 29 is to be explained by the fact

that the inner surface of such a cast of the uterine cavity is not smooth, but shows a very remarkable grooving. This has been remarked by various observers, and by some has been considered to be connected with the division of vessels. At the height of those fields formed by grooves a star-shaped, divided vessel is supposed to be found. The vessels change in the same way as in normal pregnancy. The "cell layer" is filled with a network of fine capillaries much wider than normal. The nearer we approach the deeper layers from the surface, the larger become these fine vessels, so that they are there four to five times as large. They run partly parallel to the surface, partly obliquely to it, and lie at times so close beneath it that no cell layer can be distinguished over them. While in the deeper layers their course is a twisted one, near the surface they are straight. Extra branches are not given off by the vessels. In my specimen I could see the vessels everywhere lined with a distinct en-

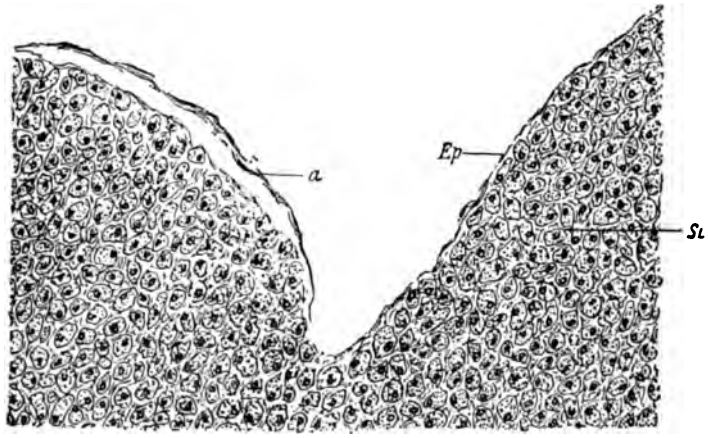


FIGURE 29.—SPONTANEOUSLY EXPELLED UTERINE DECIDUA IN A TUBAL GESTATION *(two and one-half months).*

St., stroma consisting of enlarged cells; *Ep.*, surface epithelium stretched to an endothelial-like membrane—at *a* it is loosened from the underlying tissue as a result of the cutting.

dothelium. Whether I was dealing with capillaries cannot be stated positively, for the arteries as well as the veins lose their muscular wall in the change from endometrium into decidua.

This is not the place to enter more closely into the very difficult relations; I believe I have discussed sufficiently what is important for practice.

That these relations are of great importance in practical diagnosis is shown by the fact that the microscopist is often asked whether a piece expelled from the uterus is a menstrual anomaly, or whether it is related to an abortion or to an extrauterine pregnancy. The decision of this question is of importance in many ways. Upon such a decision may depend the acquittal or condemnation of one accused of artificial abortion. Upon it depends likewise the therapeutic procedure if the

diagnosis reads "extrauterine gestation." Even though these conditions have been minutely considered in the previous discussion, a still clearer idea may be obtained if we briefly view these three conditions from the standpoint of differential diagnosis.

(ε) Differential Diagnosis between Menstrual Decidua, Uterine Decidua in Intrauterine Pregnancy (Abortion), and in Extrauterine Gestation.

In discussing the changes of pregnancy, stress has been laid upon the fact that the cells of the interstitial tissue change into the so-called "decidua cells." It must be mentioned, at the beginning of the discussion upon differential diagnosis, that the decidua cells have, as we may say, no specific signification. It is impossible to diagnose a pregnancy from the presence of these large cells alone, for, aside from pregnancy, *they may result from any irritation or stimulus which causes increased growth.* The cells of the interstitial tissue are, like the entire mucous membrane, subject to much change in their form, but return to their normal appearance, as a rule, as a result of the power of regeneration inherent in the mucous membrane of the uterus. The same is true of the epithelial cells of the glands. They take on, so long as pregnancy exists, a flattened changed form as the result of pressure; but so soon as pregnancy is interrupted and abortion takes place it does not take long before their previous form is regained. Usually we are dealing with a bleeding which has existed for some time when we are called upon to make a diagnosis of pregnancy from such uterine sheddings, and the epithelium has meanwhile had sufficient time to regenerate. Even though this were not the case, the flattened or cubical epithelial cells are quite as uncertain a sign of pregnancy as are the decidua cells. I have frequently found glands lined with such low epithelium in cases of uterine myoma. It would be sad if we wished to make the difference of a micron, more or less, in the size of an epithelial cell an important point in diagnosis.

The following drawing (Fig. 30) serves as an illustration of what has just been said. It is taken from a specimen expelled from the uterus of a patient who had bled for three weeks. Menstruation was previously always regular; only at the last period the bleeding did not cease as usual after six days, but continued, so that she was very anemic when taken into the clinic. The patient appeared so cachectic that it occurred to me, in consideration of the history, that either a benign or malignant neoplasm was present. Not the least support for the idea of an interrupted gestation was present, for the patient denied the expulsion of an ovum or of pieces of tissue.

If we observe the specimen we find the interstitial tissue changed into so-called "decidua cells"; to be sure, not of the same size at all points, but only at *c* as large as we have described and illustrated in intrauterine pregnancy (Fig. 28, *b*). Here there is also a distinct flattening of the cells. At *b*, on the contrary, the cells resemble ordinary

interstitial cells more than decidua cells. In the neighboring area also the other cells are not so large as those at *c*, and under the space *d*, filled with blood, may be seen distinct spindle cells. To the right of this blood space filled with red blood cells there are at *a* and around *a* several sections through dilated capillaries turgid with blood. In addition there is a section through the gland *e*, whose epithelium shows no flattening and

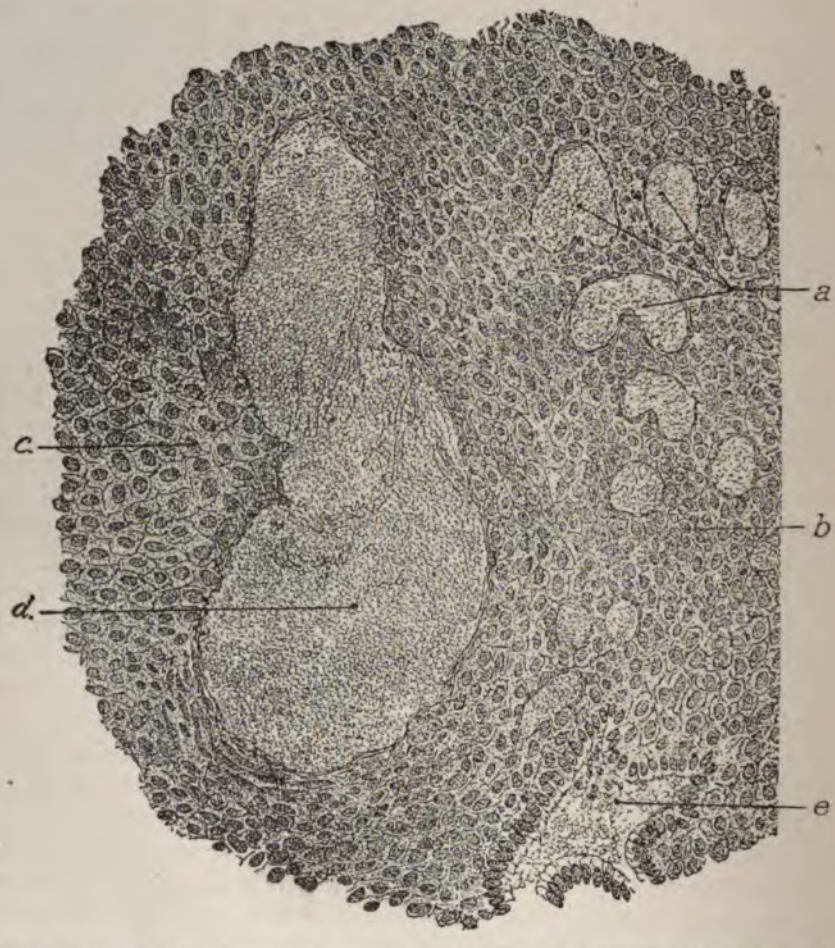


FIGURE 30.—EXPELLED PIECE OF TISSUE IN AN ABORTION *(explanation in text, pp. 85, 86).*

which is also filled with blood. I should not have considered it justifiable to make the positive diagnosis of pregnancy from this section alone, for it might just as well have been a menstrual decidua. The size of the connective-tissue cells might easily be due to a productive inflammation existing before the expulsion of the membrane. In spite of this the diagnosis of pregnancy was positively made, but was founded on the examination of FURTHER sections. These showed, in addition to

the tissue which greatly resembled a uterine decidua, other tissues of fetal origin, namely, chorionic villi.

From this we come to the conclusion that *a positive diagnosis of abortion can never be made from the uterine decidua alone, but only through the presence of tissue of fetal origin, i.e., chorionic villi.*

Since I have frequently observed during my lectures that very few know the appearance of chorionic villi, I have given in Fig. 31 an illustration, which comes from the same specimen as the previous drawing. The chorionic villi are like trees with branches and twigs, and are supposed to furnish the connection between the ovum and the uterine decidua. They consist of a stroma *(c)* and an epithelial covering *(b)*.

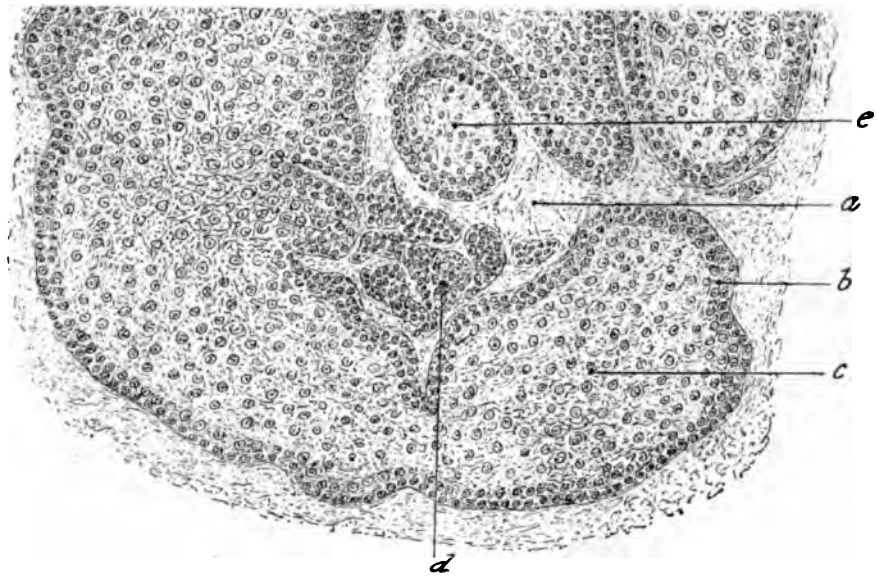


FIGURE 31.—CHORIONIC VILLI *(strongly magnified)*.

a, blood coagulum in the intervillous space; *b*, epithelium (double layer of nuclei); *c*, embryonal connective tissue of the villi (the largest villi are cut longitudinally and obliquely); *d*, section through the tip of a villus; *e*, transverse section through a villus.

The stroma is formed of embryonal connective tissue, *i.e.*, young cells or nuclei which lie irregularly in a colloid substance in which connective-tissue fibres are formed in the later months. The epithelial covering varies according to the age of the ovum. At the beginning of the second month three layers have been distinguished as clothing the villi, two of which layers are cubical epithelium (Fig. 31, *b*), the other being a very thin layer of endothelium, which is marked off from the blood in the spaces between the villi as a very thin membrane. The latter represents the endothelium of the dilated maternal blood vessels. In these epithelial cells are seen nuclei only, which are suspended in a homogeneous substance; cell borders can be distinguished only at an

early period (syncytium). In the later months there is usually only *one* layer of epithelium present, which eventually also disappears.

In the sections made through such pieces coming from an abortion we do not always get villi without other tissues, as in Fig. 31, but transverse sections through villi surrounded by the decidua cells described above; for one form of the villi, the so-called "adherent villi," are in direct connection with the decidua, in which they are planted firmly, furnishing the first union between the maternal and fetal organisms. In such specimens the villi are sharply outlined from the cells of the

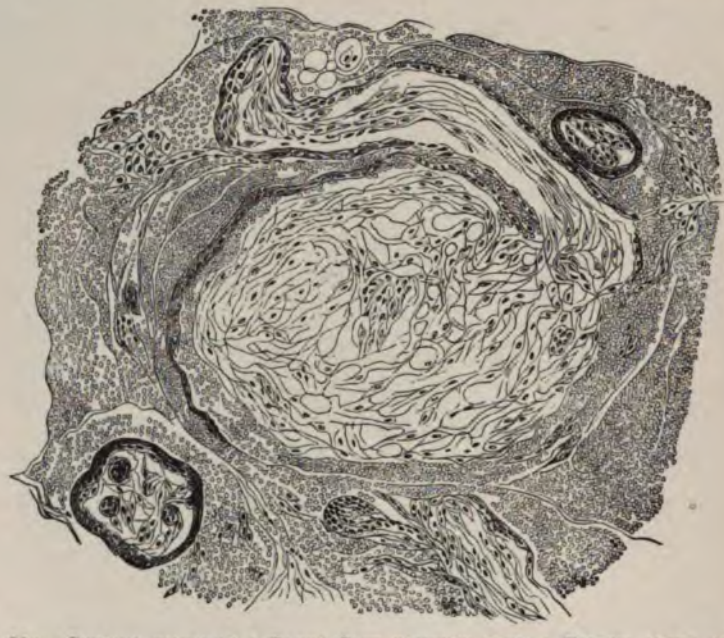


FIGURE 31*a*.—SECTION THROUGH A BLOOD CLOT REMOVED FROM A UTERUS AFTER ABORTION *(slightly magnified)*.

Transverse and longitudinal sections of villi of various sizes; below and to the right an epithelial elongation; the epithelial covering of the larger villus in the middle mostly lited off by blood. (After Orth.)

interstitial tissue, so that, once observed, doubt concerning their character can never arise.

It is, therefore, always possible, if chorionic villi are present, to recognize a piece expelled from the uterus as connected with a pregnancy, and in this way to distinguish it from the other two forms of decidua.

What is, then, the difference between the decidua cast off during menstruation and one cast off in an extrauterine pregnancy? According to my observations, which have been confirmed, a spontaneous expulsion occurs only when the "cell layer" is entirely formed, for only this is thrown off (in normal pregnancy with the ovum) here without the ovum. The fundi of the glands remain behind in the uterus, and for that reason such a decidua consists of enlarged decidua-like cells. These

are covered with an endothelial-like layer which represents the changed surface epithelium. *Glands are not present.*

In a menstrual decidua, on the other hand, the surface epithelium is present in part, and the cells are of a cylindrical form as in the normal endometrium. Although, as a result of mechanical injury, no surface epithelium may be present, glands are still always to be found, and their epithelium as a rule appears quite normal. The cells of the interstitial tissue show in most cases no other changes than those caused by the pressure of the poured-out blood. Therefore no great weight can be attached to this condition, for the cells may be changed by previous affections of the endometrium, so that all stages, from normal cells to giant and decidua-like cells, are found. Therefore the characteristic difference consists *in the presence of glands and of unchanged surface epithelium, in the one case, and in the change of this epithelium to an endothelial-like cover, and the absence of any formation which may be considered a gland, in the other case.*

It is evident that it would be wrong to curette the uterus for the purpose of making a microscopical examination in suspected extrauterine pregnancy, for in this event the deeper-lying layers would be also removed. In that way one of the important criteria for the diagnosis would be lost. From a clinical standpoint, also, such a curettage is contraindicated, since many cases are known in which after this procedure immediate rupture of the ovum resulted with fatal internal hemorrhage.

2. PATHOLOGICAL ANATOMY.

A. General Remarks.

The pathological anatomy of the endometrium, if discussed in a systematic manner, would take us too far from the practical purposes which we are following. We should lose ourselves in details which would remove us from the essential questions concerned in the subsequent portion of this book. It must, therefore, not be viewed as peculiar if we do not speak of the usual division into acute and chronic inflammations, since we are only concerned with giving those general evidences observed in the curetted particles which lead to the practical and weighty decision as to whether we are dealing with an inflammatory condition or a neoplasm, and whether this neoplasm is anatomically benign or malignant.

Test curetting of the uterine lining has without doubt furthered early diagnosis. In this lies, in all branches of medicine, an important factor in deciding therapy. Where the clinical symptoms give us no positive diagnosis, at times the removal of a small piece permits us to say, for instance, that we are dealing with a carcinoma, provided that we are fortunate enough to have found the affected area with the

curette. *A negative result in such examinations is never a positive proof.* Here, again, the deficiency of even this method may be observed, for a method can accomplish no more than is within the limit of possibility. If a small piece has been removed by the curette, we can only say that in this piece such and such changes have been found; whether other conditions exist in the uterus cannot be judged from such a specimen. It would be false to state, after examining a curetted piece in a doubtful affection of the uterine mucosa, that all doubt as to the nature of the affection has been removed. This *may be the case* if the evidences are characteristic enough to make a diagnosis positive; but *it is not necessarily so.*

Another point is this: in making a test excision from the vaginal portion we see at least the affected area from which a piece is taken. This is not the case in curetting, and, as a rule, the uterine mucous lining is removed blindly, healthy and affected areas without distinction. In the early stages, as a rule, only isolated areas of the mucous lining become affected, especially in the case of a malignant neoplasm. This appears at first as an isolated tumor, at times of microscopical size. It needs considerable luck to find, among the numerous healthy or only secondarily changed particles just removed, the area of importance to us; or else innumerable sections must be made and examined before saying that in the curetted particles positively nothing carcinomatous is present.

Since in curetting the eye is of no value, another method which will supply this deficiency in doubtful cases is certainly of importance. This means we possess in the process of *examination of the uterine cavity with the finger after its dilatation.* Unfortunately, this method is used too rarely.

When the uterus has been dilated by one method or another, so that its cavity can be palpated up to the fundus, the examining finger detects the isolated affected areas either through their hardness or softness, or other variations. At times the finger can directly loosen the brittle masses. If this be not possible we know at least at what point we should observe especial care in doing a test curettage. Even in this way, naturally, we cannot always make an exact diagnosis, for there are certain limits beyond which our microscopical knowledge does not carry us.

Nevertheless, even though a microscopical examination has furnished us with no positive evidences of one or another affection, it is still an important aid in many doubtful cases when used in conjunction with the clinical results. If, for instance, the patient is a woman who has long passed the climacterium, we know that the character of the endometrium is different from that after puberty. The glands have partly disappeared and the interglandular tissue shows an increase of the elements situated between the cells; much fibrous connective tissue is developed, and the cells, which formerly were so prominent, disappear. If, in case of sudden bleeding which is not controlled by the usual means,

a test curetting be done and a rich development of glands be observed microscopically, this fact alone, even though it does not justify immediate radical treatment, demands minute observation and further close study of the case. In other words, the microscopical examination is an exceedingly important aid *in supporting a clinical diagnosis,* even though it does not always furnish an absolutely certain result.

Another point should be mentioned. Are we able, from certain points observed in curetted particles, to say with certainty that in the examined specimen no malignant neoplasm exists, in spite of the fact that in all probability such a condition is present in the mucous membrane?

This question is justified by the following statement: It has been settled, by examination of many an entire uterus affected with carcinoma and obtained by operation or by autopsy, that very often in the circumference of a carcinoma striking hyperplastic changes in the epithelia of the neighboring glands occur. The originally simple epithelial layers increase so that the gland wall is covered with two or more stratified layers. Through pressure these epithelial cells easily lose their cylindrical form and become flat. In oblique sections such pictures result that the gland wall seems to be lined with a stratified layer of squamous epithelium. This led certain examiners to believe that such an increase of the cylindrical cells represented the beginning of a carcinoma. If such hyperplastic formations are seen in the glands of a curetted specimen we must conclude that this is not a real carcinoma, according to the usual anatomical claims, but that it may easily represent a beginning stage. Since such pictures are often found in the circumference of a carcinoma, there may be carcinoma present in the supposed case. This conclusion I do not consider justifiable, for the simple reason that such pictures are by no means characteristic, but, as we have seen before, may occur in *entirely benign changes.* I would therefore advise the beginner never to let himself be influenced to make a diagnosis which does not accord with the facts, but which is only a possibility.

As microscopists we should only judge the complete anatomical specimen before us, and make a diagnosis according to positive observations. So long as we know no characteristic etiological evidences the anatomist and the clinician frequently come into conflict. It then must be left to the experience of the clinician whether, *in spite* of the negative microscopical condition, he is to operate or not. We dare not, however, for that reason recede one step from the real basis.

After these preliminaries we are to discuss the affections of the endometrium as we generally find them in curetted particles. As a rule, a curettage of the uterus for microscopical purposes is usually done because of long-continued bleedings, *i.e.*, chronic cases. Having already discussed the conditions present in abortion, the following chapters deal only with inflammatory and hyperplastic changes and with malignant neoplasms.

B. Inflammations.

It is not always easy, and is sometimes impossible, to define the limit between inflammations and neoplasms of the endometrium. As a result of the various processes which occur the different conditions often overlap; or, as a result of the circulatory changes caused by inflammations, certain tissue forms proliferate, since the endometrium reacts energetically to every stimulus. In spite of this fact we may distinguish two forms of inflammation of the endometrium which, in their final stages at least, show special and quite different characteristics: interstitial endometritis *(atrophicans)* and hypertrophic endometritis *(fungosa)*.

Those conditions which no longer show evidences of inflammation and are probably the result of an inflammatory irritation, give in the microscopical specimen the impression of newly formed tissues, and I therefore prefer to class them with the hyperplasias of the endometrium. This may affect the glands and the interstitial tissue at the same time. We then speak of a *diffuse* and a *circumscribed* (polyposa) hyperplasia of the whole endometrium, depending upon whether the entire mucous membrane or only part of it is affected.

If, on the contrary, we are dealing with an increase of the glands alone, which in excessive cases may lead to complete disappearance of the interglandular tissue, this condition (depending upon whether the entire mucous membrane or only a part is affected) is called *diffuse* and *circumscribed* (polypoid) hyperplasia of the glands of the endometrium. Under these names are included all growths of the endometrium which are inflammatory and clinically as well as anatomically benign. For the malignant and destructive neoplasms are reserved the generally accepted and recognized names, such as *adenoma, carcinoma, sarcoma,* and the *mixed forms.* Such a clear division between benign and malignant changes of the endometrium would probably lead to a prevention of the many disadvantages which, in part at least, are caused by a confusion in the gynecological-anatomical nomenclature.

(α) Interstitial Endometritis.

As is indicated by the name, the important changes take place in the interstitial tissue. All the changes which are usually characteristic of inflammation are likewise found in inflammations of the uterine mucous membrane. The interstitial tissue, if the affection has not existed long, is infiltrated with small cells in proportion to the severity of the irritation which causes the inflammation. The round cells replace completely the original cells of the interstitial tissue in certain areas, so that the gland sections are absolutely surrounded by small-celled infiltration. In *gonorrheal endometritis gonococci are found in the interstitial tissue and in the glands.* The glands at first are only slightly changed; at most the epithelial cells in certain areas have proliferated as a result of the increased blood supply, and line the gland wall in several layers.

This is a condition found in nearly all inflammatory and hyperplastic formations of the endometrium, and has no special significance.

The following figure (Fig. 32) shows this stage of the affection, from which, after existing for a long time, other changes may result. These finally cause the entire mucous membrane to be replaced by a layer of fibrous connective tissue. Therefore the same condition results here through inflammation which we have previously learned to be a normal condition after the menopause.

Before this end-stage is reached the endometrium goes through the following changes: The small round cells gradually become many times their former size. The longer the process continues, and the more nutrition these cells obtain from the newly formed vessels (which occurs in all inflammations), the larger these cells become, so that, with their large

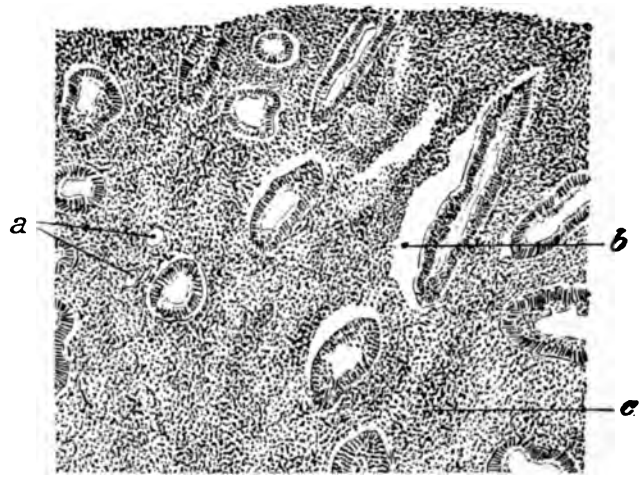


FIGURE 32.—INTERSTITIAL ENDOMETRITIS.

a, sections of capillaries; *b*, space resulting from contraction of the gland wall in alcohol; *c*, interstitial tissue everywhere replaced by a small-celled infiltration. The epithelial cells of the glands are at points arranged in many layers.

nuclei and their plentiful protoplasm, they resemble epithelioid or decidua cells. This latter resemblance has led anatomists to believe that this is a specific process of the endometrium. This is not so, for whoever takes the trouble to read in Cohnheim's text book, vol. i., page 366, the changes occurring in a productive inflammation with incomplete regeneration, will find that *such a formation of epithelioid cells is usual in such an inflammation*. Just as the formation of these cells occurs, so there may arise various transition forms, from the small round cells up to giant cells with many nuclei, to spindle-shaped cells, club-shaped cells, and cells with processes.

In examining the small curetted particles we find that the process does not attack all parts of the mucous membrane alike, nor does it run the same course in all parts, and we therefore observe the products

of inflammation in its various stages. While, in one bit which has been examined, such areas with large and spindle-shaped cells may be seen, in other pieces small round cells with regressive changes, fatty degeneration, and a destruction of cells may be observed.

The further changes go on in the endometrium in the same way as in other organs, and there results, as Cohnheim says, "the further development of the large epithelioid cells. The early round epithelioid cells send out processes, and become fusiform and stellate. The processes grow and undergo further metamorphosis, the characteristic of which is the splitting into fibres and fibrils. Since the fibres of various cells lie close together, there result bundles of fibrils to which, as a rule, several cells belong. The protoplasmic remnants which result in this formation of fibrils remain and form cells which lie between these bundles. The frame or supporting framework in which this development takes place is formed by the network of new vessels which have originated in the anastomosing vessel arches. *What, however, has resulted from this process is, when summed up, nothing more than genuine vascular connective tissue.*" Whether this view is correct or not can be proven only by further examination. I have simply quoted it to show that epithelioid cells are not formed as a specific product in the uterus alone. The only thing which must still be mentioned is the condition of the glands. These are pressed and become atrophic as a result of the continued increase of the interstitial tissue. The glands disappear from the superficial layer, which is replaced by connective tissue, and there remain only isolated atrophic gland fundi in the deeper layers of the mucous membrane. These disappear likewise when the process has terminated, so that the uterine lining is no longer a mucous membrane but a layer of fibrous connective tissue *(atrophic endometritis)*.

(β) Hypertrophic Endometritis (Fungosa).

While in an interstitial inflammation the interstitial tissue plays an active rôle, in the hypertrophic form all parts of the mucous membrane are affected. A decided thickening of the mucous membrane may result if this affection be present for a long time. The membrane grows either equally in all areas or, as is more frequent, only certain regions are affected. These overgrow the remainder of the mucous membrane and rest upon it like a fungus.

The name introduced by Olshausen distinguishes the process very well, for the microscopical changes vary so much in the different stages and according to the degree of inflammation that it is impossible to select for it a uniform title. The difference between it and the previously named inflammation consists in the fact that here no disappearance of tissue occurs as a terminal process, but, on the contrary, a growth of the same takes place. Just as the interstitial tissue is increased, so also is there a growth of the glands. They increase in number and in size, and in some places the cylindrical epithelium is found strati-

fied. Through the coexisting growth of the interstitial tissue the form of the glands is changed; the interstitial tissue forms projections toward the gland wall whereby the lumen of the glands is filled with numerous folds. In other places the interstitial tissue retracts, drawing the gland wall with it and causing dilatation of the glands. In the interstitial tissue the same processes occur as we have learned take place in interstitial inflammation. Now small round cells are seen, now spindle cells, now epithelioid cells, then again products of regressive changes such as are characteristic of every inflammation.

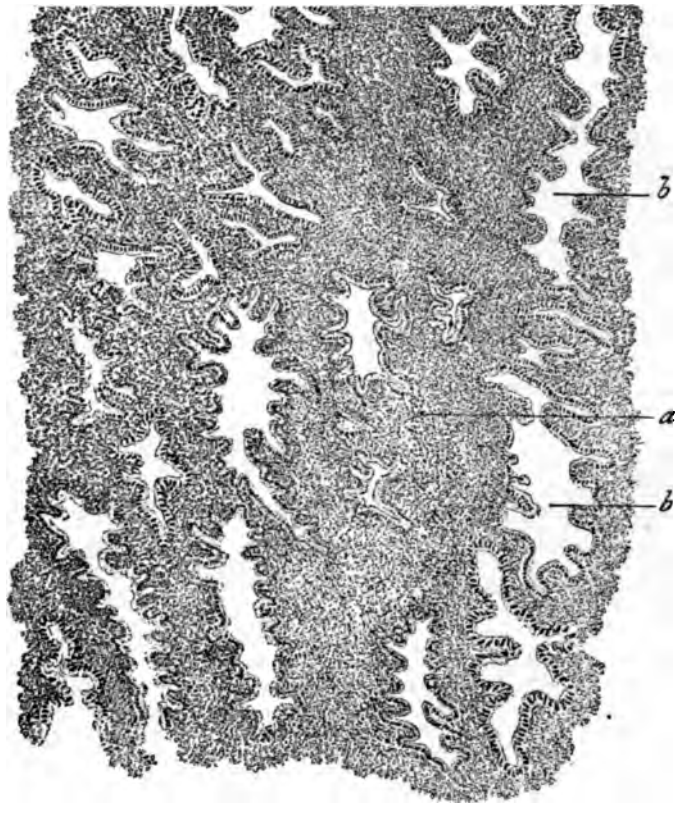


FIGURE 33.—HYPERTROPHIC ENDOMETRITIS *(Fungosa)*.

a, small-celled, infiltrated interglandular tissue; *b*, sections through dilated glands with numerous depressions.

Through the increase of the glandular epithelium an increased secretion of mucus takes place, and at times the gland lumina are filled with mucus and the excretory ducts are obstructed. If the mucus is not discharged, but is continually formed, there result cystic dilatations of the glands, and such cysts are frequently found in this form of inflammation.

Such cysts may be as large as a pinhead, so that in a microscopical section they are recognized with the naked eye, and occasionally such

sections have a sieve-like appearance. The epithelial cells are flattened by the increasing pressure and in some cases disappear, and occasionally the wall is lined with an endothelial-like membrane. The vessels take a decided part in this form of inflammation, for they also share in the general proliferation. The capillaries increase in number and in size; the plethora is considerable, so that blood is easily poured out into the interstitial tissue. This trickles partly up to the surface through the epithelium of the superficial covering, which has often already degenerated, or else it passes through the epithelium of the gland walls and fills the glands as in Fig. 34.

It is seen that in this process manifold and very different changes occur, at times coexisting, at times developing the one from the other,

FIGURE 34.—HYPERTROPHIC ENDOMETRITIS WITH BLEEDING INTO THE GLANDS.

a, small-celled interstitial tissue, with extravasations of blood in places (through the smaller, lighter cells the red blood corpuscles are seen); *b*, sections of glands filled entirely or partly with blood; *c*, invaginated gland in transverse section (the internal circle of epithelium is not entirely complete; some cells have fallen out).

and it therefore happens that the microscopical pictures are not easy to understand. The growth of the gland epithelium combined with oblique sections may be mistaken for a malignant neoplasm. The isochronous occurrence of spindle and epithelioid cells in the interstitial tissue sometimes makes a diagnosis even more difficult, yet I think that sufficient practice enables one to distinguish this inflammatory condition from a malignant neoplasm. It must be kept in mind that in just such inflammations different stages of the affection are present; and even though numerous chains of such cells be found in such a specimen, the study of many sections gives us a clear idea of the character of the entire complication. That examinations should never be confined to one or two

sections in doubtful cases is, of course, scarcely necessary to mention. In such cases it is better to embed such curetted particles in celloidin on one cork, so that a section may present six to eight different areas united under one cover-glass.

(γ) Decidual Endometritis.

Just as the endometrium may become affected in the non-pregnant state, so may it be the seat of inflammation during pregnancy and subsequently. As a rule, it is the continuation of previously existing endometritis, yet during pregnancy inflammation may also be the result of *septic* (artificial, criminal abortion) or *gonorrheal infection*. The decidua is then thickened *in toto* or shows polypoid formations *(polypoid decidual endometritis)*. The inflammation is confined principally to the interstitial tissue, and the decidua cells are pushed apart by numerous round cells or through increase of the connective tissue *(the scirrhous form)*.

Such inflammations lead to the retention of placental tissue when the ovum is expelled. Such placental remains unite very firmly with the decidua and after the termination of pregnancy may continue their growth *(placental polyps)*. Microscopically there are found in such polyps chorionic villi and the products of the inflammation just described.

C. Hyperplasia.

By hyperplasia we understand a growth of the mucous membrane in which none of the above-described inflammatory products, small-celled infiltration, etc., can be recognized. In all cases the entire mucous membrane is thickened or only parts of it. The latter form results in polyps situated on the mucous membrane, either pedunculated or sessile. If the interstitial tissue and the glands are both affected we are dealing with

(a) Hyperplasia of the Whole Endometrium,

which is of two forms:

(α) Diffuse Hyperplasia of the Whole Endometrium.

Here the entire mucous membrane is proliferated, so that the inner surface of the uterus is clothed with a thick lining. The individual elements of the mucous membrane are increased in number and size with active participation and new growth of the vessels. A uniform participation of the entire mucous membrane is here as rare as in inflammations. More frequently partial proliferation is observed, and in such cases we speak of

(β) Circumscribed Hyperplasia of the Whole Endometrium (Polyposa).

Here is found a localized growth in which all of the elements of the mucous membrane are increased in number and in size, and this growth

projects above the rest of the mucous lining like a polyp. Fig. 35 shows these relations better than can be done by description.

We see clearly the outlined polypoid formation *(a)* projecting above the surface of the mucous membrane *(b)*. In the lower layers of this mucous membrane (this is a curetted particle) it is seen that fibrous strands are present between the partially dilated glands. These bands, when strongly magnified, are seen to be muscle fibres. The growth itself is marked off from the rest of the mucous membrane by a zone of small-celled infiltration, and is therefore a pure polyp formation arising from the mucous membrane and at no point penetrating the muscular wall.

In Fig. 36 this polyp, more highly magnified, shows the following changes:

The cells of the interstitial tissue *(e)* are plainly seen to be uniformly

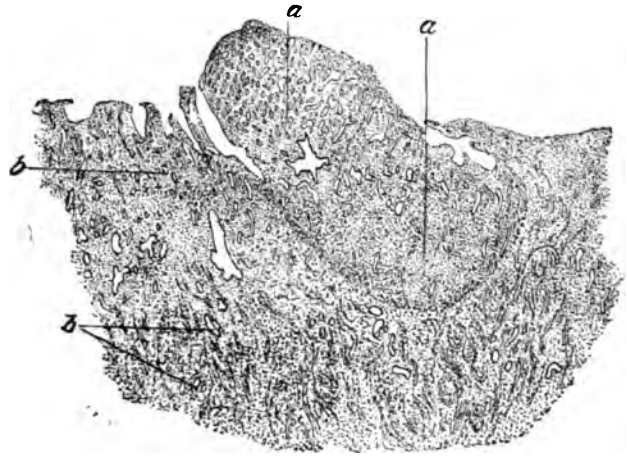


FIGURE 35.—CIRCUMSCRIBED HYPERPLASIA OF THE WHOLE ENDOMETRIUM *(Polypoid) (enlarged 4 ø)*. **Explanation in text.**

increased without the presence between them of small-celled infiltration. Although increased in number their previous form and size are well preserved. At *b* a group of large cells is seen between the other cells. This is a section through the fundus of a gland. The glands are increased in number and some of them are dilated. Their epithelium has proliferated in certain spots, so that the wall is lined with several layers, as at *d*. The most noticeable change is the presence of numerous vessels. We see arteries *(a)* and veins *(a_1)*, and also numerous sections of vessels which cannot be distinctly classified, but which are easily recognized from their structure. At *c* is seen the point of division of a vessel. This new formation of arteries and veins is always found in such polypoid formations. While in the endometrium very fine capillaries, and especially venous capillaries, are intended to carry off the blood as much as possible, here the newly formed arterial and venous branches

have a tendency to stimulate the growth of these polyps to a decided extent. The irritation caused by this new formation leads to a hyperemia of the other portions of the mucous membrane. In this way it may be understood why these polypoid formations are usually accompanied by profuse uterine bleeding.

If only the glands take part in the hyperplastic changes we are then dealing with

(b) Hyperplasia of the Glands of the Endometrium.

This is divided into two forms:

FIGURE 36.—FROM THE POLYP "*a*" IN FIGURE 35 *(strongly magnified)*. Explanation in text.

(α) Diffuse Hyperplasia of the Glands of the Endometrium.

The entire endometrium increases in thickness as a result of an excessive growth of glands. The glands are so increased that eventually the interstitial tissue is reduced to a minimum, and finally between every two glands only one layer of cells is found, and nothing of an inflammatory character is to be observed. The epithelium of the glands often covers the walls in numerous layers, but preserves its cylindrical form. These hyperplastic formations differ from the destructive glandular neoplasms in that *the glandular form is always preserved and the epithelial cells always respect the boundary formed by the membrana propria.* The whole gives an impression of regularity and reflects the *typical* gland character.

The second form represents almost the same structure, with the difference that only a part of the entire mucous membrane is concerned.

(β) Circumscribed (Polypoid) Hyperplasia of the Glands of the Endometrium.

This polypoid formation, as we have just studied it, occurs with atrophy of the interstitial tissue and consists exclusively of glands. This is a relatively frequent affection. Its finer structure is the same as that which we have explained under hyperplasia of the glands of the entire mucous membrane. The same characteristics of benignity exist in both forms, so that it is not necessary to go into further explanations. With these new formations the limit of clinically benign and anatomically homologous neoplasms is reached. As soon as the growth goes further and the borders of the different tissues are no longer respected we are dealing with a destructive neoplasm. These often cause great difficulty in diagnosis if only small particles are examined.

D. Neoplasms.

Having already divided the affections of the endometrium in a manner of practical value for our purposes, we are now to touch upon the clinically malignant neoplasms. Since the microscopical diagnosis in such cases may lead to a dangerous operation, it is clear that only such cases should be reported to the clinician as malignant and suitable for radical operations as present the strictest evidences demanded by diagnosis. In the first place, the interest of the patient demands this; and, secondly, it is to the interest of science, for if the pathologist in examining curetted particles makes the diagnosis of malignant neoplasm, and if the removed organ does not substantiate this diagnosis, it is a scientific falsification, for such cases are classed as having been cured by operation. So long as we do not know the specific cause, only the general characteristics of these malignant neoplasms hold good. If a small piece curetted from the uterus does not suffice for recognition of this affection we can only say "non liquet." It then remains for the clinician to decide what should be done. We have already mentioned that clinical observation is frequently an essential support to the microscopical diagnosis. The malignant neoplasms of the endometrium originate either from the epithelium or from the connective tissue. The epithelial neoplasms *(adenoma and carcinoma)* develop, as a rule, from the epithelium of the glands, but recent investigation has shown that they may develop from the cylindrical epithelium of the surface. The connective-tissue neoplasms *(sarcoma)* develop from the cells of the interstitial tissue.

(a) Carcinoma of the Endometrium.

For the diagnosis of carcinoma of the uterine mucosa, which is of less frequent occurrence than that of the vaginal portion of the cervix, the same rules hold good as for the latter. It would, therefore, be a repeti-

tion were I to mention again these various points. A carcinoma is always (sometimes with modifications in structure, such as cancroid, colloid carcinoma) a formation of epithelioid elements in a connective-tissue basis. The boundaries of the remaining tissue are not respected by the neoplasm, for the latter grows, in *atypical form,* into the glands and vessels without stopping at their enveloping membrane. *A piece of curetted mucous membrane is sufficient for this diagnosis,* for in the

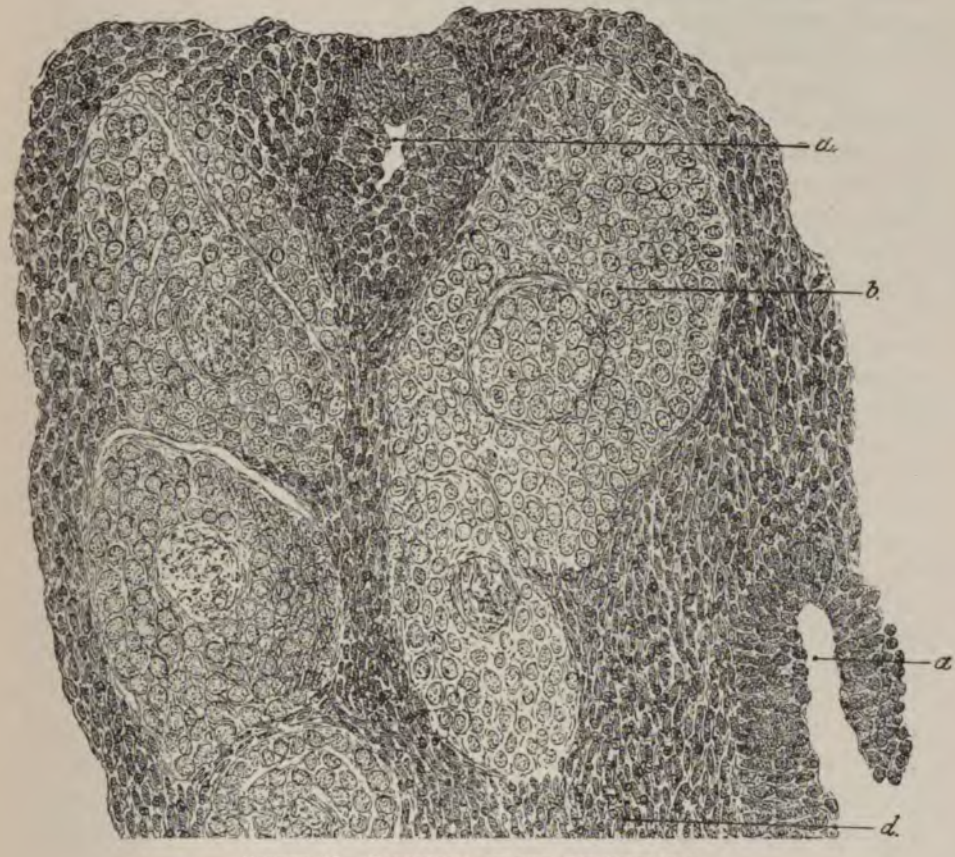


FIGURE 37.—CARCINOMA OF THE ENDOMETRIUM.

a, gland sections with growth of epithelium; *b*, carcinoma nodules; *d*, interstitial tissue consisting of spindle cells, between which scattered round cells are found.

mucous membrane are various tissues from which we may easily see the variations of a neoplasm if the structure of this neoplasm is fully pronounced. No one can hesitate to recognize in Fig. 37, a curetted particle, the presence of a carcinoma.

The drawing presents several very important and characteristic areas. We see the easily recognized cancer area *(b)* and also changed glands. In these "cancer cones" we recognize epithelioid cells of various sizes. As the lighter color of the drawing shows, they have taken on the hema-

toxylin stain less intensely than the remaining tissue and the cells lining the glands. The sharply outlined areas lying in the centre of these "cancer cones," should be noticeable, especially to the beginner.

In the cancer cone *(b)* this distinct zone represents unchanged cells, while in the other "cones" only cell detritus can be seen. Such central softenings often occur in carcinoma and are described by all examiners. Sometimes no cells or cell remnants are seen in the centre, but, instead, cavities sharply outlined by an endothelial membrane. Certain examiners consider these to be capillaries. In such a case the carcinoma would be filling the perivascular lymph vessels.

The changes in the epithelium of the glands *(a)* are important. It is seen that the former cylindrical cells line the wall of the gland in stratified layers. The form of the epithelium appears changed, and the nucleus larger than usual. This is especially the case in the gland which lies at the right hand lower corner of the drawing. In the upper gland, on the contrary, the changed form of the cells is doubtless caused by an oblique section. The growth of epithelium in the glands is an event occurring with every irritation of the mucous membrane, as has already been shown in various places. On the other hand, this growth has been considered to be the beginning stage of a carcinoma arising from the glands, so that when such changes are found in a curetted specimen a diagnosis of a "beginning carcinoma" is made. I cannot advise too much caution in guarding against such a diagnosis. I agree with Orth when he says, in discussing the diagnosis to be made from small bits of tissue, that "the presence of irregular alveolar cavities filled with epithelial cells, or of reticular epithelial cords, perhaps with pearls, is proof of a carcinomatous neoplasm and demands total extirpation; while, on the other hand, *various forms of proliferation in the glands, situated in the general tissue* groundwork, twistings, dilatations, formations of papillary protruding folds in the lumen, and even the filling of the lumen with cast-off cells, do not of themselves permit a positive diagnosis of malignant neoplasm."

A sufficient proof of the malignancy of the process, if typical alveoli are not present, is furnished if these growths of the epithelium do not take place inside the glands, but BREAK THROUGH THE MEMBRANA PROPRIA and penetrate into the interstitial tissue; and yet I mention again that before the diagnosis of a perforation through the membrana propria is made, all means at our disposal must be used to determine whether we are not dealing with an illusion caused by the plane of the section.

(b) Malignant Adenoma of the Endometrium.

The diagnosis of an adenoma in an excised uterus is not difficult. We are then dealing with a tumor formation which is made up of glandular structures, consisting of tubes lined with cylindrical epithelium placed next to each other with very little supporting material and not confined

to the mucous membrane alone, but either continued further into the underlying muscle, and in older cases sometimes even breaking through the peritoneum, or else continued irregularly in the muscle as nodules of the same anatomical character. When of long-standing, there results the formation of solid epithelial strands, so that we are no longer dealing with a pure adenoma but with an adenocarcinoma.

The diagnosis from curetted particles is more difficult, *and at times impossible.* As we have seen, there occurs at times with pure hyperplasia of the glands a very excessive increase in their number. What has already been shown is that this latter form always preserves *the original gland type.* In the case of a destructive adenoma we are dealing no longer with glands but with epithelial strands. These retain at the beginning a lumen, but assume *atypical shapes* which no longer resemble the uterine glands, *possess no membrana propria, and lie close together.* Ziegler says: "The microscopical examination of small pieces can define the neoplasm, in that the tissue of an adenoma follows the gland type, but does not reproduce exactly the type of glands normally found in the organ concerned." Orth says: "The discovery of glandular tubes lying close together, especially when the normal boundary formed by a tunica propria and longitudinal muscle fibres is absent, is in my opinion enough to justify the diagnosis of malignant neoplasm and to indicate the need of total extirpation."

I would mention, as especially characteristic, the fact that in such adenomata we are no longer dealing with the original ciliated cylindrical epithelium of the uterine mucous membrane. The epithelial strands consist of closely grouped cubical cells which are rounded like an egg and are frequently irregular in form. The small nucleus lying usually at the base is decidedly enlarged at the expense of the protoplasm. The cells lie irregularly next to each other, without showing a defined line of demarcation from the interstitial tissue.

The clinical condition is an essential support to the microscopical diagnosis in this case. If, in examining the uterine cavity with the finger, a soft, circumscribed tumor is felt, from which brittle pieces may be loosened, and if these pieces show the microscopical condition just described, we are justified in undertaking a radical operation. The subsequent examination must then decide whether the previously diagnosed form of neoplasm was present. If, however, a circumscribed tumor be not felt and we are perhaps dealing with the affection in its first stages, then the microscopical examination does not suffice, since in curetting we cannot remove the deeper layers of the muscle without danger of perforating the uterus. *The deep extension of the glandular neoplasm into the muscle is, then, the only criterion of the malignancy of the neoplasm.*

It has been claimed by Ruge and others that it is often too late to prevent recurrence if this last criterion is always waited for. This may be true, but, on the other hand, we must consider that if the uterus

be removed because of a diagnosis of "beginning malignant adenoma" (pure growth of glands without the typical formations of carcinoma), and then no area is found in the excised organ which substantiates the first diagnosis and the patient does not suffer from a recurrence, no proof is furnished that a malignant neoplasm has been removed.

In my opinion *this diagnosis, as well as the diagnosis of sarcoma made from curetted particles, is the most difficult* which has to be made in this line. Even the most practised and one who has had great experience *can make these errors.* We are often compelled to say that in the pieces given to us for examination we do not find the necessary evidences of the presence of a malignant neoplasm. The clinician, on the other hand, will, in spite of this, as a result of his experience and his observation, remove the organ and find a well-defined malignant neoplasm. And the opposite is just as likely to occur. *As yet our microscopical knowledge of the first stage of these changes is not sufficient to justify an absolute decision in all cases.*

(c) Sarcoma of the Endometrium.

The same difficulties confront us in the diagnosis of a sarcoma as in the case of an adenoma. Here also, if a large tumor is at our disposal for microscopical examination, a diagnosis can be made without difficulty according to the recognized criteria, for it is a tumor rich in cells, which, according to our present views, has developed from the cells of the connective tissue. According to the form of the cells we distinguish *round-celled, spindle-celled,* and *giant-celled* sarcomata. It should not be understood that the tumor must consist exclusively of one or the other form of cells, for usually the various cell forms are present, of which only one is especially marked. The uterine glands are generally destroyed in the sarcoma, so that the tumor consists entirely of cellular elements and vessels.

With reference to the seat of origin we distinguish two forms, sarcoma of the mucous membrane and sarcoma of the wall.

(α) Sarcoma of the Mucous Membrane.

The mucous membrane is either completely involved by the neoplasm *(sarcomatous degeneration),* or there results a circumscribed tumor. The latter are usually polypoid formations which fill the uterine cavity and may enter the vagina through the cervical canal. By edematous infiltration or myxomatous degeneration there may result here, as in the cervix, *the grape-like sarcomata.* In these are found both glands and cysts; as a rule the glands are destroyed relatively early. The neoplasm originates from the cells of the stroma, which take on most varying cell forms. Most frequently round-celled sarcomata are observed.

(β) Sarcoma of the Uterine Wall.

The sarcomata which begin in the wall of the uterus are, as a rule,

sarcomatous degenerations of myomata *(myosarcoma)*. Their malignancy is shown by the sudden rapid growth and by the formation of localized metastases in the early stages. The location at first corresponds to the seat of the myoma. Then the sarcoma grows toward the uterine cavity and a sanious degeneration of the surface layers occurs. On the peritoneal surface of the uterus are formed numerous nodules, which extend to the parietal peritoneum and cause metastases in other organs. These sarcomata are usually spindle-celled. They are derived from the muscle cells or the cells of the interstitial connective tissue or the endothelium of the vessels.

Since these sarcomata of the uterus are usually malignant and quickly cause an enlargement of the organ by their infiltration of the wall with tumor nodules, *the existence of such a clinical and microscopical condition* makes the diagnosis quite certain. The diagnosis from a curetted particle without any clinical evidence is uncertain, for we have seen that the cells of the interstitial tissue may take on all possible forms in an inflammation. At any rate, it must be mentioned that, as a rule, different stages of inflammation are present at the same time, such as degeneration, etc. The sarcomatous neoplasm, on the other hand, is free of any inflammatory mixture. An especial proof of the anatomical malignancy of the process is the existence of areas in which the sarcoma breaks into glands or vessels.

The condition of the glands is important, as in inflammation of the interstitial tissue the glands usually show no or else unimportant changes, whereas in sarcoma they may be destroyed relatively early.

(d) The Destructive Neoplasms Arising in Connection with Pregnancy.

The tumors of the uterus arising in connection with pregnancy have caused considerable discussion in later years. To simplify matters, I would recommend, in agreement with Waldeyer, the following classification: According as the neoplasm takes its origin from maternal or fetal tissue, we distinguish deciduoma or chorioma.

(α) Deciduoma.

As we have seen, destructive neoplasms may take their origin from the endometrium. The same may occur when the endometrium has been changed by pregnancy into a decidua. If the neoplasm originates from the epithelial elements of the decidua (gland fundi), there is formed a *carcinomatous or adenomatous deciduoma.* If, on the contrary, the neoplasm originates from the connective-tissue elements, there is formed a *sarcomatous deciduoma.*

These tumors are then to be considered as ordinary sarcomata or carcinomata which occur during or after pregnancy. On the other hand, those tumors of the gravid uterus which originate from the fetal elements (chorion) form a separate group.

(β) Chorioma (Waldeyer).

Sänger was the first to call attention to this affection and to recognize it after like cases had been described by R. Maier. At the time of the publication of the first edition of this book only a few works concerning this subject had been published, but in later years a large amount of literature has appeared, more than one hundred separate articles. In spite of this fact there is no agreement with regard to the histogenesis of the tumor, so that my observation of four years ago, to the effect that many questions connected therewith remain to be answered, holds good to-day.

In chorioma we are dealing with a tumor which develops in connection with pregnancy (abortion), from the chorionic villi, and which, through early metastases into other organs, usually leads to an early death. The propagation of these metastases occurs, as a rule, through the blood channels. According to a table of Eiermann, of thirty operated cases, six remained free from recurrence after two years or more. This shows that it is possible to operate in time, if only the diagnosis is made sufficiently early. This is possible, from our present knowledge of the neoplasm, by comparing the clinical and the anatomical conditions.

In the microscopical picture are found cords and strands of protoplasmic masses with numerous nuclei and vacuoles (syncytial masses), which branch frequently and are connected with each other in a reticular manner. This forms larger and smaller mesh spaces, in which various large cell elements with large nuclei, and also polynuclear giant cells, are present. In the tumor are found many blood extravasations into the tissue and numerous irregularly formed spaces which are to be considered as blood spaces. In addition necrotic areas are usually present. These are remains of the syncytial trabecular formations, whose outline can no longer be recognized, but whose nuclei are preserved.

Clinically it should be mentioned that the growth of this tissue does not take place mainly toward the uterine cavity, as in sarcoma and carcinoma, but toward the uterine muscle. Gottschalk was the first to give a very exact microscopical description of this neoplasm. He found, in a case, distinctly recognizable chorionic villi and these same structures in the metastases. The villi showed their connective-tissue centre as well as their syncytial (epithelial) covering. Since the connective-tissue centre was richer in cells than normally, he, in agreement with Waldeyer, laid great stress upon this fact and considered the neoplasm to be a sarcoma.

This evoked contradiction from other examiners, who believed that the tumor originated from the epithelial elements of the chorionic villi, and for that reason considered it to be a carcinoma. This is the general opinion at the present time, the result especially of the works of L. Fränkel and Marchand, which view is also shared by Ruge. Whether this view is correct in all cases seems to be doubtful; at any rate, the credit due Gottschalk in recognizing this condition cannot be diminished.

With regard to the histogenesis of the neoplasm, it cannot be said with certainty whether we are concerned with an epithelial or a connective-tissue formation, until complete light is thrown upon the origin of the layer which covers the villi.

As yet this has not been done. On the contrary, we find diametrically opposed opinions. According to my investigations, which were made on very young placentæ in cases of tubal gestation, the covering of the villi in their earlier stages is made up of three layers (see Fig. 31). The stroma of the villi, made up of embryonal connective tissue, is covered by a double layer of round cells. This is of *ectodermal* origin and must be considered the double epithelial coating of the villi. Upon this lies a layer of long cells, which, in my opinion, represent the *endothelium of the maternal blood vessels.* This is pressed forward into the intervillous blood spaces by the growing villi like the fingers in a glove. If this external covering of the chorionic villi is not fetal but maternal, it belongs nevertheless topographically to the villus, and must be considered as belonging to it. Pfannenstiel has expressed the opinion that this layer, originating from the endothelium of the vessels, forms the subsequent syncytium; the above-mentioned double cell layer lying underneath it becomes later a single layer (the layer of Langhans) and represents the epithelium of the villi. This view may be accepted.

It is seen that the origin of tumors of the chorionic villi may vary. If only the epithelium is taken into consideration the neoplasm must be reckoned with the carcinomata; if the tumor originates from the stroma of the villi it is a sarcoma, and if the epithelium is also affected it is a sarco-carcinoma.

If the tumor is derived from the syncytium we may call it *chorioma syncytiale,* or, in consideration of Pfannenstiel's view, *chorioma endotheliale,* reckoning the syncytium topographically as part of the villus, although we admit that genetically it belongs to the maternal part of the placenta.

In the numerous descriptions in the literature, and in comparing the same with my specimens, it seems clear that we are dealing with a specific neoplasm of the chorionic villi, but that from case to case we must decide whether the same is a carcinoma, a sarcoma, or a mixed tumor. For that reason Waldeyer proposes to call this neoplasm *chorioma,* whereby it is simply said that all the elements which compose the villus may be concerned in the neoplasm. The name chorioma seems to me the most suitable, in that it mentions the characteristic feature. Under chorioma come those cases in which the connective tissue of the stroma is concerned in the growth, as well as those cases which consist mainly of syncytial or epithelial (the layer of Langhans) growths. If the microscopical examination decides from which part of the chorionic villi, in any case, the neoplasm originates entirely or in part, we may call it *chorioma carcinomatosum, sarcomatosum* or *sarco-carcinomatosum*

or *syncytiale endotheliale.* The difference of opinion concerning the origin and make-up of the tumor may be seen in the various names which I have gathered together from historical interest:

Deciduoma malignum, sarcoma deciduo-cellulare, sarcoma of the chorionic villi, sarcoma of the chorion, malignant placental-villous tumors, sarcoma chorion-deciduale, deciduo-sarcoma uteri giganto-cellulare, serotinal tumor, carcinoma syncytiale, choriocarcinoma, syncytioma malignum, epithelioma syncytio-ectodermale or epithelioma ectodermo-syncytiale, epithelioma ectodermale.

With regard to the diagnosis I should like to mention the declaration of Sänger "that it is always necessary to examine the uterine cavity with the finger after dilatation of the cervix, which is another ground for giving up the objectionable, uncertain, and dangerous curetting of the uterus for retention of membranes, as is usually done." It is, therefore, advisable, as I have often pointed out, to accept the view that *the tactile examination of the uterine cavity is an important aid in deciding the meaning of the microscopical condition.*

(e) Tuberculosis of the Endometrium.

Though tuberculosis of the endometrium belongs primarily to the rare cases, it occurs occasionally. The clinical symptoms are such that the distinction between it and a malignant neoplasm is not always an easy task. In the microscopical examination of a piece of mucous membrane we find the well-known tubercles with giant cells which we have illustrated in tuberculosis of the vaginal portion of the cervix, in which it is sometimes possible to stain the tubercle bacilli.

Naturally, if we do not obtain a positive result at first, numerous sections must be stained, for the presence of tubercle bacilli is undoubted proof. If, however, they are not found, the anatomical structure of the tubercle is sufficiently characteristic to prevent confusion with other affections. The interstitial tissue shows either decided small-celled infiltration with hyperplastic formations of gland epithelium, in the early stages, or else it changes to granulation tissue with simultaneous atrophy of the glands. If the diagnosis tuberculosis is made, radical operation should follow, just as with malignant neoplasms, providing that other tubercular involvements can be excluded. But even if a slight affection of other organs is present (glands, lungs) we may yet hope that, after checking the loss of blood due to tuberculosis of the endometrium, the affection of the other organs may be more easily healed.

B. THE WALL OF THE CORPUS UTERI (MYOMETRIUM).

1. Inflammation (Metritis).

In the connective tissue situated between the muscle bundles in-

flammation may occur, usually coming from the endometrium, in rare cases from the serous covering of the uterus. In acute inflammation there is a large accumulation of leucocytes, which force the muscle bundles apart and cause, by serous transudation, a doughy swelling of the uterus. One of the most frequent causes of this affection is gonorrhea, but it may also be caused by septic infection.

In these cases there may result the formation of abscesses in the wall, sometimes of great size. By a demarcating suppuration, a large portion of the wall may be thrown off (metritis dissecans), this usually bringing about the process of healing.

Chronic inflammation leads to the development of much connective tissue between the muscle fibres, which become more and more atrophic the longer the process lasts. Eventually the entire muscle may disappear and the uterine wall, thickened by the formation of connective tissue, is changed into a hard mass. In this way certain bleedings may be explained, for the blood vessels, which are usually compressed by the contraction of the muscle, gape in the inflexible connective tissue, which possesses no contractile power.

2. Neoplasms (Myoma, Fibromyoma).

In the wall of the uterus myomata find their principal seat. They originate directly from the muscle and are situated either directly under the mucous membrane (submucous myoma) or deeper in the wall (interstitial, intraparietal, or intramural myoma), or, finally, close under the peritoneum (subserous or subperitoneal myoma). The first and last forms may become pedunculated and form polyps. The intramural myomata may occur in various portions of the wall at the same time and cause, as is well known, immense tumors. Histologically speaking, pure myomata rarely occur. Connective tissue is always found in addition to muscle fibres. The endometrium shows, as a rule, changes of a hyperplastic character, especially a decided increase in the glands.

Not infrequently epithelial formations are found in the myomata. These originate either from the *uterine glands,* which then show cystic dilatation, or else are to be considered as *remnants of the Wolffian body and duct* (v. Recklinghausen). (See page 161.)

Various changes may occur secondarily in myomata. There may occur edematous infiltration of the myoma, accumulations of fluid in the dilated lymph spaces (lymphangiectatic fibromyoma, fibrocysts). In place of serous fluid the tumor may show extravasations of blood in its interior (cavernous fibromyoma).

There may also occur fatty, hyaline, or myxomatous degeneration, or necrosis or suppurative degeneration of the myomata. In the latter case, as in metritis dissecans, whole layers may be expelled, causing much difficulty in the way of microscopical diagnosis. Finally, calcification of the myomata must be considered. Either calcium concretions are found

in the interior of the myoma or there is formed a more or less complete calcium shell around the tumor.

That myomata may undergo sarcomatous degeneration has been already mentioned under sarcomata. In this way mixed tumors result, especially if in a myoma glandular structures are also present (adenomyosarcoma). From this form a carcinoma may develop, which is also to be considered a mixed tumor (adenocarcinomatous myoma).

V. TUBES.

1. NORMAL ANATOMY.

(A) Position and Course.

The Fallopian tubes, also called oviducts, are tubes which furnish the connection between the ovary and the interior of the uterus, and are designed to convey into the uterus the ripe ova expelled from the ovaries. The tubes are organs symmetrically arranged, and begin their course from both corners of the uterine fundus. After they penetrate the mucous membrane they pierce the muscle wall of the uterus in a slight arch, ascending a little from their origin at the mucous lining, and then run nearly parallel to the upper surface of the uterus above the round ligament into the abdominal cavity. Here the tubes keep this course for a short distance and then make a horseshoe turn backward and downward, so that the abdominal opening, with its adjacent ovary, lies more posterior than to the side of the uterus. This normal situation of the tube was first shown in the excellent topographical representations of His and Waldeyer. Only by considering this situation as the normal can a clear idea of the occurrence of many pathological processes be gained. The picture which has appeared in all text books, in which the tubes, with the broad ligaments of the uterus, bounded the latter like the wings of a butterfly, tended to give a false impression of the normal situation of the sexual organs. For instance, it was impossible from such an illustration to understand how the so-called "external migration" of the ovum could take place. It is necessary in making a bimanual examination to know where the tubes and ovaries are supposed to be. In my lectures I have frequently had the opportunity to see that beginners had a false idea of their relations.

(B) Classification of the Various Sections of the Tube.

We distinguish in the tube an interstitial portion, the isthmus, the ampulla, and the fimbriated end (infundibulum).

By the *interstitial portion* we mean that part which runs through the uterus. It is distinguished from the uterus as a distinct annular

structure perforated by a canal as fine as a hair. This canal is considerably narrowed by longitudinal folds, which in this portion are unimportant, but which through the formation of accessory folds become more numerous the nearer we approach the abdominal end. The muscle in the interstitial part appears to consist of a layer of circularly arranged fibres, while a longitudinal layer is not present. The mucous membrane consists of a thin layer of round cells, and has an epithelial covering of ciliated cylindrical cells, which likewise cover the mucous lining of the entire tube. The movement of the cilia is from the abdominal end toward the uterine ostium.

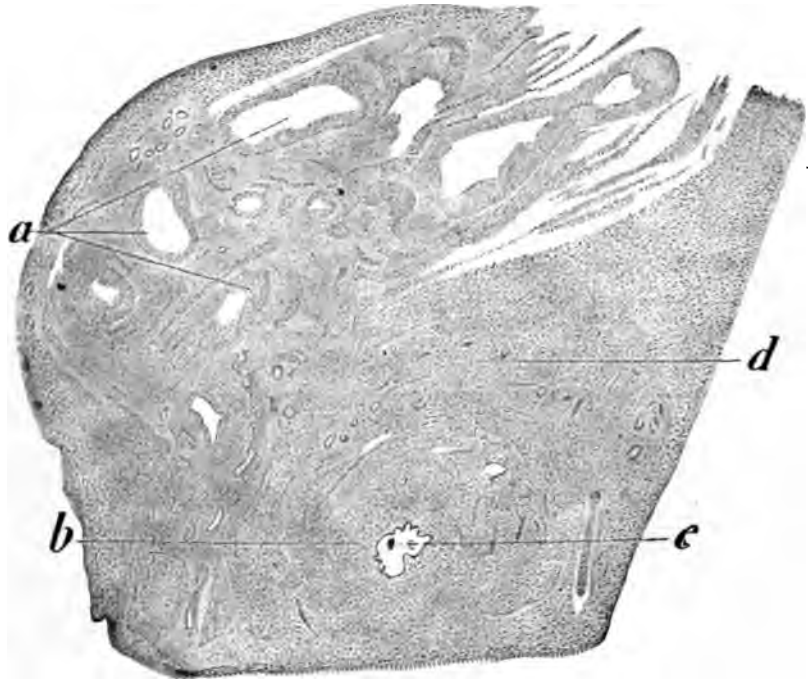


FIGURE 38.—INTERSTITIAL PORTION OF THE TUBE.

Below the large vessel lumina *(a)* (branches of the ovarian artery and vein) is seen the annular tube *(b)*. The lumen is lined with cylindrical epithelium. The structures *(c)* in the tube lumen are sections of folds; *d*, muscle of the uterine fundus.

After leaving the uterine wall the tube runs as an independent structure in the upper angle of the broad ligament, and appears as a smooth round cord of the thickness of a lead pencil at the uterine end, while at the abdominal end its circumference is twice as great. The average length of the tube is ten to twelve centimetres, but variations occur.

The *isthmus* of the tube, as the part from the uterine border up to the point of turning is called, is distinguished from the so-called "ampulla" only by the slighter development of the individual layers. The structure of the wall is the same in both parts. From without inward we

distinguish a serous covering; a layer made up of loose connective tissue in which the large vessels run, and generally called subserosa; the muscularis and the mucous membrane. It should be mentioned that the connective tissue of the ampulla is richer in cells. The folds here are larger than in other parts of the tube.

The serous covering is as firmly united to the underlying layer as is the case in the body of the uterus, and for that reason it can be peeled off with difficulty. Upon this covering is a densely branching net of lymph vessels (Poirier).

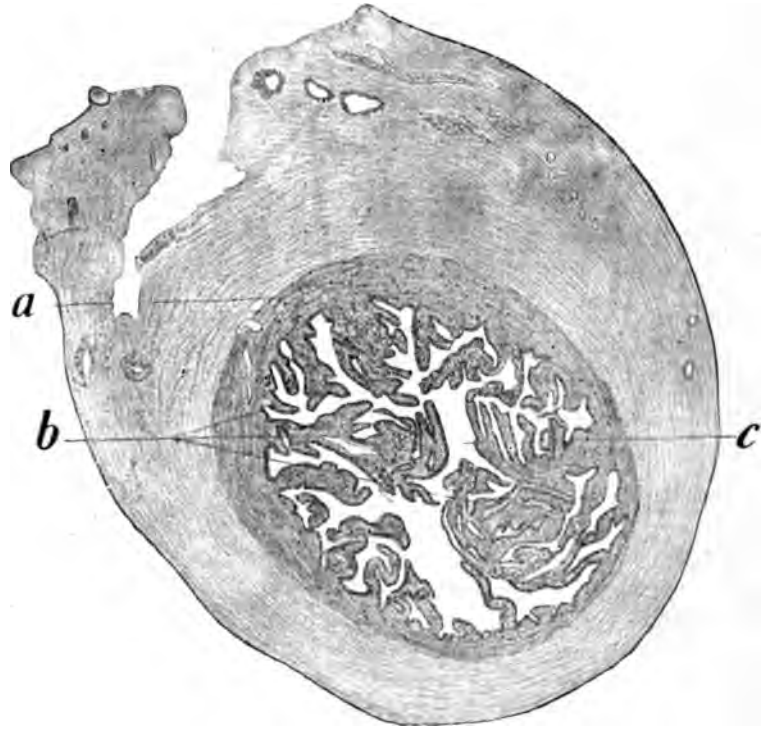


FIGURE 39.—ISTHMUS OF THE TUBE *(near the ampulla)*.
a, muscle; *b*, folds; *c*, tubal canal.

The muscle consists of an external longitudinal and an internal circular layer. The latter sends extensions to the mucous membrane, to the four principal folds which extend along the entire length of the tube. No muscle fibres extend to the finer divisions of these folds. The muscular development is relatively weaker at the abdominal than at the uterine end. The increase in thickness of the abdominal end is caused only by the numerous ramifications of the mucous membrane folds. Between the muscle bundles are found everywhere bundles of loose connective tissue in which the muscles and nerves extend to the mucous membrane.

The mucous membrane is situated directly upon the muscle, so that, as in the uterus, no submucosa exists. The cells which lie in the mucous membrane of the tube resemble the stroma cells of the uterine mucous membrane, but are smaller than these and lie very close together. Between them lies a very delicate connective-tissue meshwork. The stroma cells give the impression of lymphoid cells.

The mucous lining of the tube does not bound the canal in a straight, even surface, but forms longitudinal elevations. In the region of the abdominal opening these elevations with their small accessory folds reach such a high grade that one can no longer recognize a central canal. In

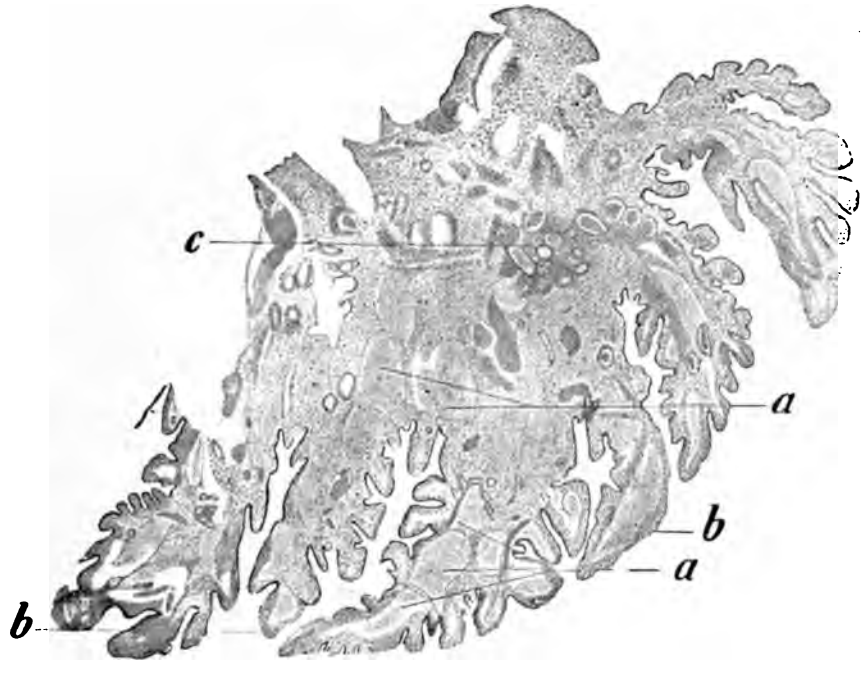


FIGURE 40.—FIMBRIATED END OF THE TUBE.

Blood vessels *(c)*; lymph vessels *(a)* dilated. The epithelium at certain points *(b)* is absent.

transverse section one gains the impression of villi with numerous branches extending toward the tube lumen from all sides of the mucous membrane. Through adhesion of these numerous accessory folds, and by oblique sections, pictures easily result which may be mistaken for gland sections. It must be held in mind that in the normal tubal mucous lining *neither glands nor villi* are present.

The covering of the mucous membrane is formed by a very regular ciliated cylindrical epithelium. The cells are somewhat thinner than those of the uterine mucous membrane, but not so long as those in the cervical.

The blood capillaries extend up to the epithelial covering. The finest branches of the lymph vessels have been seen here as well as in the uterine mucous membrane. It is believed that simply tissue spaces are present, which only in the deeper layers unite to form lymph vessels.

At the abdominal end the tube is open. The numerous folds of mucous membrane project from the interior and surround the opening like a ruffle, forming the so-called "fimbriæ." One of these folds runs like a gutter to the ovary, the so-called "fimbria ovarica." The abdominal opening is not round, but oblique, and deepened like a funnel, and for that reason is called "the infundibulum." At the time of expulsion of the ripe egg an increased flow of blood to the tube takes place, and it is said that the funnel-shaped opening approaches the ovary on this account. It is the mission of the fimbria ovarica to conduct the ovum into the funnel, which is accomplished entirely by the movement of the cilia. It is therefore seen that the arrangement is such as to facilitate, as much as possible, the entrance of the ovum into the tube.

(c) Changes Occurring within Normal Limits.

The same changes as we have seen in the uterus, where the anatomical structure is liable to certain changes according to the age of the individual or during menstruation or pregnancy, occur in the tubes. It may be said at once that these changes are like those in the uterus, but of less intensity.

(α) Menstruation.

According to present investigations, it may be granted with certainty that at menstruation plethora exists. There results, though to a very slight extent, an effusion of blood in the tubal mucous membrane and the trickling of the blood into the tubal canal. Whether menstruation of the tube occurs, without uterine menstruation, seems doubtful, for we must consider that the results and observations concerning this question have always been derived from pathological cases. Experimental examinations with ligation of the tubes at one or both ends have proved that secretion by the epithelium of the mucous membrane does not normally take place. Whether such a secretion occurs during menstruation has not yet been proven—*i. e.*, under normal conditions. We are always limited, in judging these things, to observations after operation, where we are usually dealing with decidedly pathological states. At any rate, it has been observed, for instance, in stitching the stump of the tube into the wound, that at the time of the menses, at very regular intervals, the excretion of mucus or blood took place. I myself observed after a vaginal extirpation of the uterus that several weeks later a rather severe bleeding from the vagina took place. Since a secondary hemorrhage could not occur, and since the time corresponded to that at which menstruation usually occurred, it seems probable that the menstrual congestion showed itself through such an effusion of blood from the tube. Nevertheless I would reject all these observations as

absolute proof of the existence of tubal menstruation under normal conditions.

(β) Senile Changes.

After cessation of menstruation, and as age advances, the tubes show certain senile changes. They are characterized by the shrinking of the connective tissue, a shrinking of the entire organ, and a decrease in the number of folds. The epithelium is preserved longest, even though the cells become individually smaller. The cilia likewise disappear.

(γ) The Changes in Pregnancy.

During pregnancy the tube hypertrophies in all its parts, the mucous membrane with its folds increasing especially. The vessels show a decided increase in size, especially the veins and the lymph vessels. Especial changes of the individual tissues, such as the transformation of the uterine lining into decidua, do not seem, according to our present knowledge of normal intrauterine gestation, to occur in the tubes. Cases have, however, been described in which the connective-tissue cells of the tubal mucous membrane became enlarged and resembled the uterine decidua cells. With involution of the uterus involution of the tubes also occurs.

2. PATHOLOGICAL ANATOMY.

(A) Malformations.

Only those malformations will be mentioned which are of importance in practice. In the first rank are:

(α) Infantile Tubes.

Freund has pointed out the meaning of this condition in relation to the occurrence of tubal gestation. As is known, the tubes in an embryo show numerous spiral twists, which gradually disappear as the tubes and ovaries descend into the pelvis, so that at puberty there are none in the normal tube.

It is not infrequently observed that *such spiral rotations of the tubes persist after full development of the genitalia and after puberty,* in the absence of other pathological changes. Freund has given these cases the name of infantile tubes, and has repeatedly observed that the fecundated ovum is prevented by such twistings from entering the uterus, so that a tubal pregnancy results. Though some have doubted these claims of Freund, my own experience has confirmed them repeatedly. *The infantile tube is certainly one of the causes of tubal pregnancy.*

(β) Accessory Tubes and Tubal Ostia.

In addition to the normal ostium abdominale of the tube, accessory openings have been observed, which likewise are lined with fimbriæ. According as these openings lie immediately *in the tubal wall,* or are *connected with it by a pedicle,* which may or may not possess a canal, we

speak of an accessory ostium or an accessory tube. As a rule, these openings lie near the ordinary abdominal ostium, but may occur even midway between the abdominal and uterine ends. Recently I had occasion during a myoma operation to remove a tube which showed an accessory tube of almost the same length as the normal one. This showed, in addition, the peculiarity of being divided at its middle into two parts, of which one joined the wall of the tube about one centimetre from the abdominal end, the other quite near the uterine extremity. These accessory openings or tubes may communicate with the real tubal canal or end blindly. If a fecundated ovum makes its way into such a blind canal, it is clear that if the ovum develops an extrauterine gestation occurs. From these malformations are to be distinguished:

(γ) Hernial Dilatations (Diverticula) of the Tubal Canal.

It occurs, though rarely, that canals lined with epithelium pass out in a straight or twisted course from the mucosa and penetrate the muscle more or less deeply, sometimes ending under the serosa. Such a canal may take a course perpendicular to the tubal canal and then bend on reaching the muscle, running for a certain distance parallel to it.

These malformations also may furnish the cause of tubal pregnancy. In discussing these conditions, those so-called "supernumerary tubes," of which a few cases have been observed, must be kept in mind. We are dealing in these cases, as a rule, with a third tube connected with a third ovary or an ovarian tumor. These have been described as separated from the genitalia and adherent to the omentum or other abdominal organs. Whether these were originally connected with the genitalia and were freed from them later by inflammatory changes cannot be decided. Finally, in considering these malformations, I would mention a very frequently occurring formation known as

(Δ) Pedunculated or Morgagni's Hydatids.

These are small cysts of the size of a pea or walnut, filled with a clear fluid, which are either directly connected with the fimbriæ or united to them by a longer or shorter pedicle. Opinions differ regarding their origin. The real cysts are said to be lined with the same epithelium as the fimbriæ. No special pathological value is attached to these structures. (See Part III.)

(B) Tubal Gestation.

(a) Causes.

The fecundated ovum may, under certain pathological conditions, be retained in the tube and there continue its development. As causes for this abnormal insertion of the ovum may be considered, in addition to those previously mentioned *(malformations* and *arrests of development)*, all those changes which make the tube more or less impassable through

destruction of the cilia, and which make the transference of the ovum by this means impossible. Contractions of the tube muscle (peristalsis) alone are not able to move the ovum through the tube into the uterus. For this, as is generally agreed, the movement of the cilia from the abdominal to the uterine ostium is necessary. The cilia may disappear as a result of *affections of the tubal mucous membrane.*

Another, and no doubt frequent, cause of tubal pregnancy is *perisalpingitic change.* As a result of this, various parts of the tube become adherent to each other, to the uterus, the ovaries, the intestines, the omentum, and other organs of the abdominal cavity, contracting and twisting the canal so that it is absolutely impassable. In rarer cases obstruction of the canal by *polyps of the mucous membrane or tumors of the tubal wall* has been given as the cause. Some authors place *certain tumors in the abdominal cavity,* which compress the tubal canal, in a causal relation to tubal pregnancy. These permit the small spermatozoa with their active movement to pass through, but prevent the passage of the fecundated ovum toward the uterus. *The most frequent cause is an affection of the tubal mucous membrane* (often gonorrheal).

(b) Places of Insertion of the Ovum in the Tube.

After exit of the ovum from the ovary, it must pass through the entire length of the tube, and may, if any of the above-mentioned conditions are present, remain in any portion of it and continue to develop. We therefore distinguish *interstitial pregnancy, tubal proper, ampullar,* and *infundibular.* In addition to these four main forms, of which the development of the ovum in the isthmus portion of the tube is the most frequent, transitions may occur, such positions being occupied by the ovum from the beginning or the transition forms occurring during its development. An interstitial pregnancy may occur at the boundary between the tube and the endometrium, and we then speak of a *tubo-uterine pregnancy;* or at the abdominal end, when it is called a *tubo-abdominal pregnancy.* Finally, the insertion of the ovum may occur at the *fimbria ovarica,* as has been positively demonstrated.

Certain changes peculiar to pregnancy take place in the tube as soon as a fecundated egg is implanted in it and undergoes development. These correspond *only in part* to the changes which we have learned in discussing uterine gestation. The differences are the result of the essentially different structure of the tubal lining and the tubal wall. The latter is constantly stretched by the growing ovum, and finally forms only a connective-tissue wall such as results if the tube be changed to a cyst by other pathologically retained contents (serous fluid, blood, pus). The originally hypertrophic muscle disappears. In a more advanced tubal pregnancy we can for that reason recognize, as a rule, no tubal tissue, and this was the reason why so much was formerly said about "abdominal gestation." Only through examination of the early stages

have we come to recognize that almost all these cases originate in the tube.

The changes which we are now to discuss refer, therefore, only to the first weeks or months of tubal gestation. The further pregnancy advances the more do these characteristic changes disappear, quite in contrast to what takes place in the uterus.

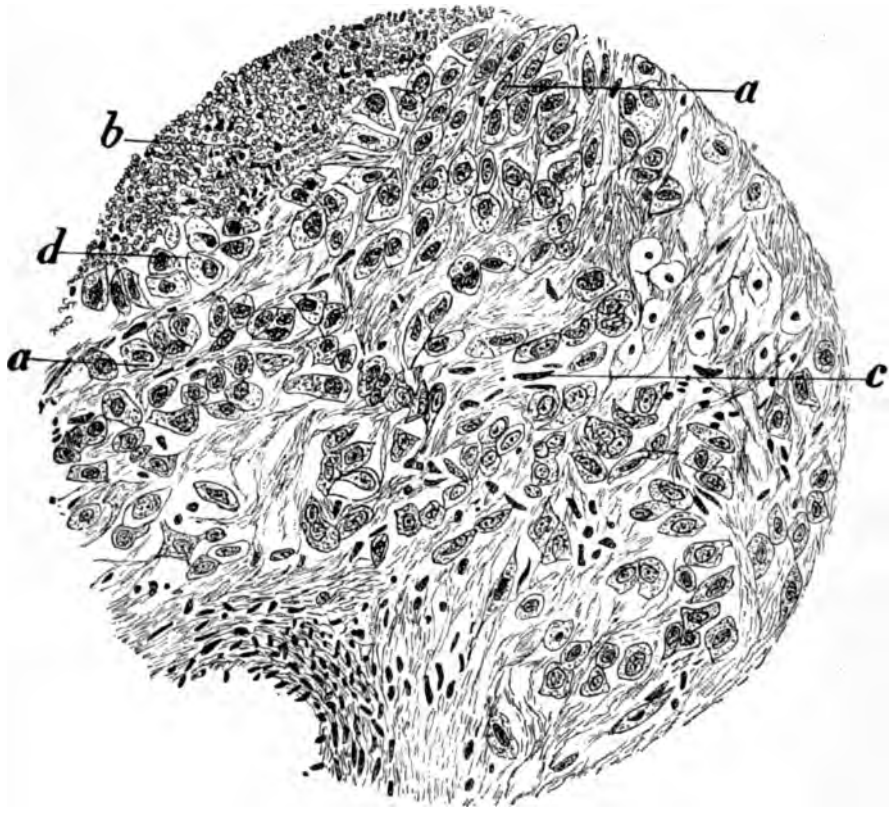


FIGURE 41.—CHANGE OF THE TUBAL MUCOUS MEMBRANE TO A DECIDUA.

a, decidua cells; *b*, round cells; *c*, spindle-shaped connective-tissue cells; *d*, intercellular spaces.

(c) Changes in the Tubal Lining in the Region of the Ovum in Tubal Gestation.

(α) Decidua Basalis of the Tube (Serotina).

All examiners agree that at the point where the ovum rests the mucous membrane cells change into decidua cells. Although they do not reach the size of the uterine decidua cells, they resemble them very much in form. The cells have a delicate, transparent protoplasm and one or more relatively large nuclei, which distinguish them from squamous epithelium. They do not lie so closely together as in the en-

dometrium, where in the upper layers they form the so-called "compact tissue," but show between them cell spaces which are filled with a homogeneous substance. Between the decidua cells are frequently seen spindle-shaped connective-tissue cells of the ordinary size, and cells resembling the normal connective-tissue cells of the tubal lining, as well as numerous round cells. We thus gain the impression that the change of the tubal lining to decidua is not so complete as in the uterus. I could not prove in any case that the division into two layers, a compact and a spongy one, occurred, as we found to be the case in the uterine decidua.

This is highly improbable when we remember that the spongy layer is formed by the dilated fundi of the uterine glands. We have seen that in the normal tubal lining no glands are present. There is not the slightest reason why we should assume that glands or gland-like structures should be formed during pregnancy, for the fundi of the glands in the uterus, which are preserved during pregnancy, serve to regenerate the glands of the endometrium and the epithelium of the surface after expulsion of the compact layer. In the tube, however, conditions are different. Glands are not formed, and the epithelial cells, which are lost at the point of insertion of the ovum and in its entire circumference, are regenerated by the growth of the neighboring epithelium, which, as we shall soon see, takes no part in the changes of pregnancy. Even though Webster describes and shows the same changes in them as occur in the uterine epithelium, I take it for granted that in this case an unusual condition was present. In general we must consider that such a stratification of the mucous membrane does not occur, but that, although the change of the tubal lining into a basal decidua is present, it is not so complete as in the uterus. Concerning the character of the epithelium at the point of insertion of the ovum opinions differ. According to my investigations the same changes occur here as in the placental area in the uterus.

The epithelium becomes flat, disappears entirely in places and is replaced by the proliferating endothelium of the maternal blood vessels. This extends upon the villi and probably forms their syncytial covering, and at the same time the inner lining of the intervillous spaces. The adherent villi pass directly into the tubal decidua, are surrounded by the decidua cells, and thus form an intimate connection between the fetal and maternal organisms. At the same time, proof is here furnished that the entrance of villi into glands is not essential for the development of an ovum.

(β) Decidua Vera of the Tube.

In the region of the fetal sac a decidua vera is doubtless formed at the beginning. It is liable to certain fluctuations in size. As a rule, *only a small annular band around the lumen or only a part of the mucous membrane of one side* undergoes decidual changes. The degree of

development of the decidua also shows individual fluctuations. Of course, all these conditions are confined to the early stages of pregnancy, so that it must first be settled whether the same stages were under examination by the various authorities who have found differences; for with the further growth of the ovum such a pressure is exerted that after a very short time many of the details described above can no longer be recognized. The structure of the decidua is the same as that of the basal decidua, so far as the decidua cells are concerned. In no case could I find a spongy layer. The epithelium is somewhat flattened by the pressure of the ovum, and no cilia appear to be present.

(γ) Decidua Capsularis of the Tube (Reflexa).

If many differences of opinion concerning the presence and the extent of the decidua exist, this is to a still greater degree the case concerning the capsular decidua. Most authors absolutely deny its existence. According to most recent investigations, I must take it for granted that *only at the very earliest period can a capsular decidua be present.* It disappears at a very early time, which explains the differences of opinion. In the capsular decidua the decidua cells described above are also present, but between the cells there is much more intercellular substance than between the cells of the basal decidua. According to Webster, there is present a profusion of vessels, especially in the region of its transition into basal decidua. At times small arteries and veins are near the base and at the pole, forming capillary spaces (Eugen Fränkel). On the outer surface there are found in spots remnants of the original epithelium which lines the tubal membrane; these are cubical or flat or are in a stage of degeneration. The greater part of the outer surface shows complete degeneration of the epithelium.

(d) The Tubal Wall in the Region of the Fetal Sac.

The changes affect essentially the muscle. It is very important to distinguish the different stages. At the earliest period there is certainly an hypertrophy and hyperplasia of the various elements, and the muscle cells increase in size as in the uterus. Very soon, however, the pressure of the growing ovum causes an atrophy of the muscle with simultaneous growth of the connective tissue. In the region where the placenta becomes adherent this hypertrophy of the muscle persists the longest, while on the side opposite the insertion of the ovum a very early thinning of the wall takes place.

(e) Chorionic Villi.

To prove the presence of a tubal pregnancy it is necessary here, just as in the uterus, to show the presence of chorionic villi, *i.e.*, structures belonging to the fetal organism. Frequently, in an operation for tubal gestation, neither fetus nor placenta is found in the tube, but there is an extravasation of blood which dilates the cavity and is firmly

adherent to one part of the wall. In such a case the presence of the decidua cells in the tubal mucous membrane is not enough to prove that a pregnancy in the tube had occurred. By thorough examination of the blood coagulum, after previous hardening of the entire specimen, we almost always find at the adherent portion of the coagulum characteristic chorionic villi.

(f) The Portion of the Tube at a Distance from the Fetal Sac, and the Tube of the Other Side.

Outside the limits of the fetal sac I was unable to find changes in any part of the tube on the pregnant side which could be considered as

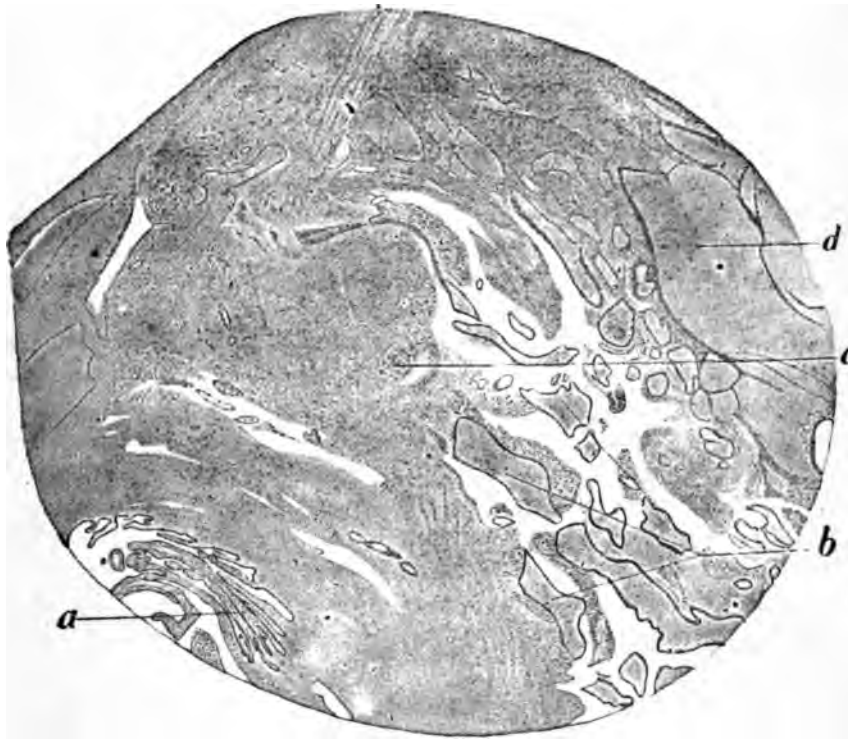


FIGURE 42.—SECTION THROUGH THE AREA OF INSERTION OF THE OVUM IN A GRAVID TUBE, WHICH AT *a* INCLUDES A PORTION OF THE TUBE WITH NORMAL FOLDS WHICH LAY OUTSIDE THE FETAL SAC.

a, transverse section through normal tubal mucous membrane—the folds are covered with epithelium; *b*, chorionic villi; *c*, decidua; *d*, blood coagula.

dependent upon pregnancy. The same is to be said of the tube of the non-pregnant side.

(g) The Results of Tubal Gestation.

It is known that ova which undergo development in the tube may grow to full term and are therefore viable. Such observations are be-

coming constantly rarer since we have learned to regard the presence of a tubal gestation *in the same light as a malignant neoplasm* and have learned to operate as soon as possible.

In most cases there is an early interruption of the pregnancy, which may take place in various ways. Every such accidental interruption is connected with danger to life. It frequently happens that the tubal wall cannot resist the pressure of the growing ovum and *ruptures.* The ovum, *i.e.,* the fetus, enters the abdominal cavity and decided bleeding takes place from the placental area and the tubal wall. This blood becomes encapsulated and forms an *hematocele,* or a *continued internal hemorrhage* takes place. Rupture usually takes place in the early months.

Just as in intrauterine pregnancy the whole ovum may be expelled through the cervix, so here the entire ovum may be expelled through the fimbriated end into the abdominal cavity *(tubal abortion).* This termination may be attended by the same dangers as rupture, but as a rule it is less dangerous.

Through hemorrhage into the sac destruction of the ovum and resorption of the embryo may result. We then have an *hematosalpinx,* which under some circumstances may lead to secondary hemorrhage.

Finally, I would mention that after tubal abortion retained placenta and decidua may form the same sort of *placental polyps* as in the uterus, and these may cause continually recurring bleedings into the abdominal cavity. I have endeavored in the above review to give a brief description of the anatomy of tubal gestation. To those who are interested in the details of this important affection I recommend the work of J. Clarence Webster.

(c) Disturbances of Circulation.

As a result of the rich supply of blood vessels in the tube, especially at the abdominal end, and as a result of their being embedded in a very loose cellular tissue, effusion of blood may follow the rupture of these vessels when they are strongly distended. This is the case to a very slight degree in menstrual congestion, as we have already said, but it happens that in congenital *(gynatresia)* or acquired closure of the tubes and the uterus the extravasated blood cannot flow off or be completely absorbed, so that by the continuation of this condition the canal of the tube is filled more and more with blood. Then the tube changes to a cyst filled with blood, which at times may reach a great size.

This condition is called hematosalpinx. This may result from *injuries* which the patient has suffered during menstruation, a fact as yet only slightly regarded. I have seen a young girl, who was thrown from a horse during menstruation, showing in the next few days a swelling of one tube of the size of a fist with symptoms of collapse.

The danger that such tubes, turgid with blood, may rupture and lead to hemorrhage into the abdominal cavity is relatively great, because of the anatomical changes caused in the tubal lining and muscle by such effusions of blood.

The hemorrhages into the mucous membrane lead to destruction of the stroma of the mucosa and the epithelium. Destruction of the muscle results from pressure of the constantly increasing blood clots, so that in extreme cases only a thin membrane separates the blood from the abdominal cavity. This, however, is not, as in the thick walls of ovarian cysts, made up of firm connective and elastic tissue, but consists of a membrane in which few elements can be recognized. The cells have been for the greater part destroyed.

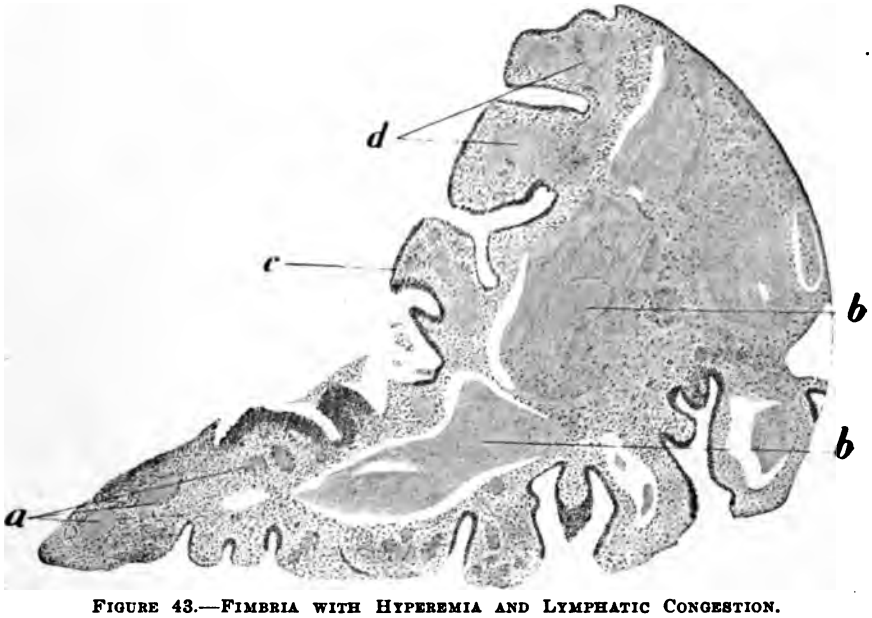


FIGURE 43.—FIMBRIA WITH HYPEREMIA AND LYMPHATIC CONGESTION.

a, turgid blood vessel; *b*, strongly dilated lymph vessels filled with lymph, which at *d* extend up to the epithelium *(c)*.

So long as there are only partial hemorrhages into the mucous membrane and muscle, as is the case in acute infectious diseases, poisoning, and acute inflammations, a restitution may take place. If, however, a large portion of the mucous lining and muscle is destroyed by the effusion of blood, then a restoration to the original condition is impossible. The most favorable result then is that the blood coagulum may become fully organized into connective tissue.

For the sake of completeness I should like to add that such bleedings into the tube have been observed in cardiac affections. An hematosalpinx *may occur secondarily* through hemorrhage into a tubal sac which is filled with serous or purulent fluid. Such a hemorrhagic fluid is also found in *malignant neoplasms* of the tube. With congestion of the

blood vessels there may occur, at the same time, congestion of the lymph vessels. Fig. 43, which shows these conditions very clearly, is taken from a case suffering from carcinoma of the vaginal portion of the cervix. The adnexa of both sides were removed with the uterus. In fimbriæ of both the vessels were turgid with blood and the lymph vessels exceedingly dilated, lymph having in part entered into the tissue. As a cause for this condition the sudden interruption of circulation by ligation of the vessels must be accepted. At the same time, this case furnishes proof of the sensitive manner in which the vessels react to trauma.

(D) INFLAMMATION.

(α) General Remarks.

Before considering the anatomical changes occurring in inflammations of the tubes it is advisable to discuss the nomenclature of these affections. Recently every one who has worked in this field has felt it his duty to invent a new name, and we find among others pyosalpinx, tubal sacs, tubal tumors, etc. One would imagine that every author wished to distinguish some point by his title; but this is not the case, for all these names denote the same macroscopical condition. I emphasize the word macroscopical. All these names seek only the characterization of what is found on bimanual examination. It is, however, impossible, or almost impossible, to draw from the clinical examination a definite conclusion as to anatomical character of an individual case. Very different causes and pathological processes lead in tubal affections to the same clinical condition, and even if we see the tumor after operation it is often difficult to decide by simple inspection which special form of the affection is concerned. This is, then, the work of the finer microscopical examination. For that reason it would be of general interest if a uniform expression for this condition were selected. The title "sactosalpinx," used by Martin in his text book, is just as good, and just as bad, as the name "tubal sac," for at times we feel a decided swelling of the tubes without their necessarily possessing any contents. As a result of chronic inflammation thickenings of the wall result, even greater than the thickness of a thumb. These may make the canal narrower than under normal conditions, and there is then no increase in its contents. For such a condition the above name is not suitable. I suggest, therefore, for swellings of the tubes observed clinically the simple expression, "tubal tumor," *i.e.*, a swelling of the tube. If the ovary cannot be isolated we have a tubo-ovarian tumor. Further classification is left to the microscopical examination.

Almost the same conditions are found in the accepted microscopical names. So many divisions and subdivisions have been artificially made

that a specimen, if we follow such a scheme, often belongs in several categories. For this reason I suggest the simple division into

CATARRHAL SALPINGITIS AND PURULENT SALPINGITIS

with their resulting conditions, which we are to discuss directly. The attempt to divide inflammations according to the causal element is impracticable and incorrect; for various causes, especially the bacterial, lead in the end to the same anatomical condition, from which it is impossible to say with certainty whether the bacterium coli, streptococcus, or pneumococcus, etc., has caused the affection.

If, as in the uterus, the inflammation of the mucous lining claims our special attention, we must not neglect the tubal wall and the serous covering; for it is not uncommon that the mucous membrane is secondarily affected, and that the infectious process makes its way from without inward. Especially must we remember that adhesions with the tubes may very easily result from affections of the serous covering of the uterus (perimetritis). Through the perisalpingitic strands resulting from these there occur torsions and displacements of these organs, and in this way the basis for the occurrence of an inflammation of the mucous membrane is furnished. The next result of an inflammation of the mucous membrane is usually swelling of the folds, and hyperemia, which first occurs in the numerous blood vessels of the abdominal end of the tube, causes serous exudation which leads to adhesions of the abdominal opening and may result in complete closure. The same holds good for the uterine opening, but here, as a rule, closure occurs later. By the forcible stretching which the tube undergoes in the course of such an affection, the entrance to the uterus is mechanically so narrowed that even in the absence of real adhesions the exit of fluid is impossible.

After these general remarks we turn our attention to the two forms of inflammation with their anatomical peculiarities and the resulting conditions.

(β) Salpingitis Catarrhalis.

In catarrhal inflammation we may distinguish an acute and a chronic stage. The cause of the purely catarrhal inflammations is to be sought, in the first place, in *mechanical disturbances.* These may arise from needless manipulations of the uterus, as in operations, massage, and venereal excesses. This explains the inflammation resulting from the severe congestion which takes place in the genitalia during coitus. It has also been observed that, as a result of *medicamental injections* into the uterus, fluid has entered the tubes and caused inflammation, the result of this irritation. In existing *endometritis,* with growth of the mucous membrane, an obstruction to the uterine ostium of the tube may occur. Since there is usually hyperemia of the other genitalia in

inflammation of the uterus, there occurs in such cases a secretion in the tubal canal and a stasis of this secretion.

Whatever may be the cause of acute inflammation, the evidences are the same as in other organs. As a result of hyperemia we find the numerous round cells in the tissue, so that its normal elements are completely overwhelmed by the round cells. The result is a swelling of the folds in the tubal lining, which lie close together and easily become adherent. The epithelium of the surface is usually intact, but we see the round cells forcing their way through the epithelium at many points and lying in the canal, which is narrowed by the swelling.

FIGURE 44.—SWOLLEN FOLDS OF TUBAL MUCOSA WITH DECIDED ROUND-CELLED INFILTRATION WHICH IN PART EXTENDS INTO THE MUSCLE. THE EPITHELIUM IS INTACT.

The process does not usually extend deeper. Now and then we see strands of round cells following the vessels in the muscularis. As a rule, the hyperemia affects the serous covering, and the peritoneum looks very red and swollen, and shows numerous signs of inflammation, leading to the formation of fine membranes. In this way long-standing inflammation leads to adhesion of the tubes to neighboring organs.

In the same way adhesions of the various parts of the tube with each other are formed, so that we find twistings and turnings of the tubal

canal. In long-continued cases the catarrhal inflammation causes *a firm closing of the abdominal opening,* because the swelling pushes the fimbriæ close to each other, causing finally a mutual adhesion. *Then begins the chronic stage,* for the tube, closed at both ends, gives no outlet to the secretion resulting from the hyperemia, which constantly collects in the tube and which may grow to very large size. I have frequently observed cases in which the tubal tumor reached up to the umbilicus. First the mucous membrane and then the muscle becomes atrophic from the pressure of the growing tumor, and it is certainly on account of the presence of numerous elastic fibres in the tubal wall that such swellings can exist for a certain period without bursting. At times it hap pens that such tubal tumors filled with serous fluid, when they reach a decided size, empty through the uterus, only to fill again in a short time. Landau, following the analogy of the conditions observed in the kidneys, has named this condition *intermittent hydrosalpinx.* The fact that the contents are always serous is characteristic of this process, but rupture of vessels occasionally occurs and the serous contents are mixed with blood. Another characteristic of hydrosalpinx is that in a short time the entire tube may become affected, so that we are dealing with a large cyst which may be fully emptied by puncture or incision at one point. Hydrosalpinx is usually one-sided, but bilateral affections are not rare.

Through the invasion of pyogenic bacteria, either from the intestines or from the uterus, a hydrosalpinx may become a tubal abscess, but it seems, from my observations, that this is a rare occurrence. *Purulent inflammations usually develop as such from the beginning,* and cause essentially different pathological conditions from those resulting from the simple catarrhal form.

(γ) Salpingitis Purulenta.

The purulent inflammation is the kind most frequently observed, especially the chronic form. An acute purulent tubal inflammation can usually be examined only in the cadaver, since these cases, as a rule, are not operated upon. *We wait until the acute process has run its course before we operate,* and we attempt the various conservative therapeutic procedures before we remove an organ of such value to the organism.

There is a greater tendency for this purulent inflammation to become chronic than to heal completely. The anatomical changes which we are now to discuss are found in cases which have come to operation after existing many years. This is the difference between this form of inflammation and the catarrhal, for in the latter there is usually a restitution, *i.e.,* healing. It is relatively rare that the catarrhal form changes into the purulent, yet such cases occur, especially if an infection be added to an existing catarrh. The cause of a purulent inflamma-

tion is *exclusively bacterial infection.* The septic and gonorrheal forms are the most frequent. In comparison with these, infections due to other bacteria are relatively rare. Among them may be considered the pneumococcus (Fränkel) and the bacterium coli.

Septic inflammations are mostly puerperal, yet they may occur through infection during operations upon the uterus, or through propagation of a bacterial affection of the abdominal cavity, such as perityphlitis, etc. At times in gonorrheal affections a mixed infection may occur.

FIGURE 45.—CHRONIC SALPINGITIS WITH EPITHELIAL INVOLUTIONS SIMULATING GLANDS *(a).*

b, tubal canal partly filled with pus.

The acute stage differs very little in its early period from that of catarrhal inflammation. The formation of pus occurs early, so that the tubal contents consist no longer of serous fluid, but of purulent secretion. On account of the numerous cells which this pus contains we usually are dealing with a thick, tenacious, and sometimes cheesy substance. In acute cases it is possible to distinguish the two main forms of inflammation by finding either gonococci or streptococci. If this is not the case we recognize the *septic* inflammation, as a rule, by the fact that it quickly makes its way deeper down, and numerous round cells are found in the muscle and under the peritoneum, while the *gon-*

orrheal inflammation remains confined to the mucous membrane. This statement, to which Martin and Orthmann call attention, I have always been able to confirm in my specimens.

In purulent inflammation there is a marked infiltration of the mucous membrane with round cells and a coexisting hyperemia of the vessels. The folds swell and become adherent or are united by the pus found between them. The cilia of the epithelia disappear, but I should like to call attention to the fact that, in spite of long-continued suppuration, the epithelium of the tubal lining is usually preserved, even on the sur-

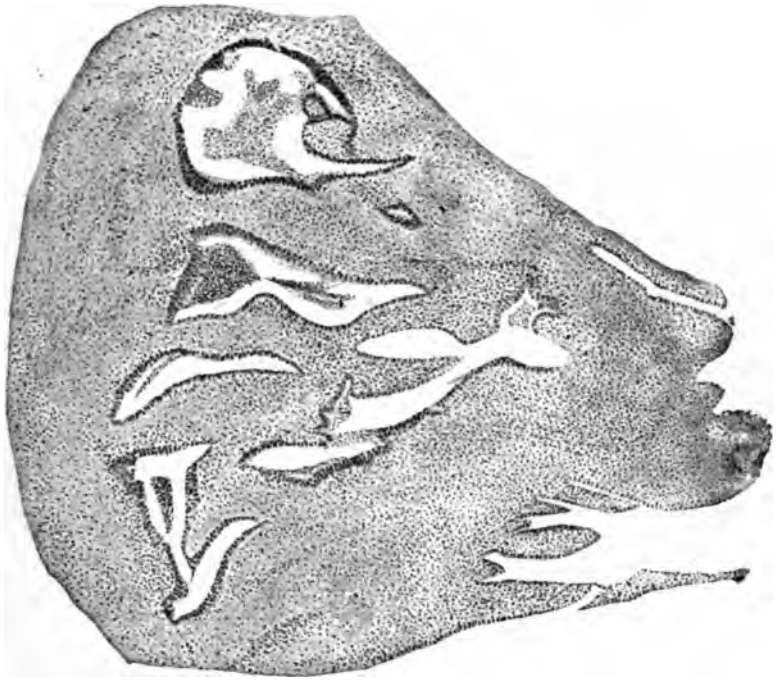


FIGURE 46.—CHRONIC PURULENT SALPINGITIS.
Section through the fold adhesions, more highly magnified than in Fig. 45.

face, which is certainly in contact with the pus, and we find only here and there certain areas denuded of epithelium.

If the acute stage has gone over into a chronic one these adhesions and unions of the folds become constantly firmer and furnish remarkable pictures, for sections of epithelial spaces result which look like glands. These pictures are naturally the more complicated and the more difficult to judge the larger the number of folds originally present, especially in the ampullar end.

In careful examination of such a specimen it may be found that the gland-like formations *are always on the surface of the mucous membrane* and never penetrate into the muscularis. If they do, we have no

longer a simple inflammation, but a neoplasm. This will be discussed later on. If we examine sections through these fold constrictions with a high power, we see that they show most varying forms, which their origin easily explains.

According as the folds have lain more or less close to each other, the sections through the spaces lined with tubal epithelium are either very narrow or wide. Through the marked accumulation of pus, the section gives us the impression that we are dealing with a cyst formation. If the section is oblique we may see curiously branching canals. If only the tops of the epithelial cells are cut it seems as though we were dealing with atypical epithelial growths.

FIGURE 47.—CHRONIC PURULENT SALPINGITIS *(hyperplastic)*.

a, thickened and united folds of mucous membrane; *b*, pus between the folds; *c*, small-celled infiltration of the upper layer of the mucous membrane.

As a rule, the changes are simpler the more simple were the original normal conditions in the tube. Nevertheless the entire picture is in general the same. It must be mentioned here that the chronic purulent inflammations cause entirely different conditions from the catarrhal form, for in the latter a large tube sac is formed after a time in which the entire tube is uniformly affected; in the former this is not the rule. In purulent inflammation *the tube is divided into different abscess cavities* by adhesion of the various parts, so that in longitudinal section through the whole tube we see several cavities of different sizes completely separated from each other. This is the reason why such a chronic purulent salpingitis cannot be healed by simple puncture or incision. This could only be accomplished if a single tube abscess were present, such as happens occasionally. More of this later on.

The anatomical changes which the tubal lining undergoes in a chronic

inflammation are, *mutatis mutandis,* the same as in every other chronic inflammation in any other organ. Through the continued irritation hyperplastic formations may result which affect chiefly the mucous membrane. Then we see the thickened folds lying close to each other and filling the tubal canal. The stroma of the mucous membrane consists partly of round cells and partly of granulation tissue, and the vessels are increased. In the narrow spaces between the folds pus is seen, which consists of closely gathered round cells, bacteria, and often also red blood cells. We are dealing, therefore, with a productive inflammation.

With the exception of the cilia, the epithelium remains intact in the chronic forms for an astonishingly long time, and in the deeper folds

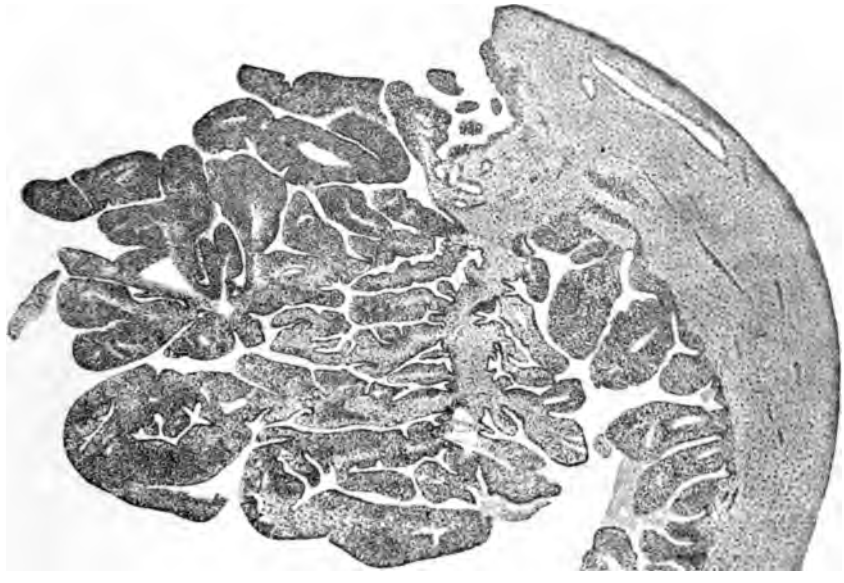


FIGURE 48.—CHRONIC PURULENT SALPINGITIS.

Marked round-celled infiltration of the folds. Superficial epithelium absent in many areas.

even the cilia are not infrequently preserved. At times cases are observed in which large areas of the surface are robbed of their epithelium without my being able to find a plausible reason for this circumstance.

Just as an hypertrophy of the folds may result, so an atrophy of the folds and the mucous membrane may be found in a long-existing case, especially if new quantities of pus are constantly being produced.

This happens either through mechanical pressure exerted by the accumulation of pus or through direct purulent degeneration of the tissue. In these cases we see, as in Fig. 49, in place of the numerous folds, the cavity taken up by the pus, between which isolated epithelial areas represent the remnants of the folds. Toward the tube wall also there is very little of the real structure of the mucous membrane to be

recognized, and we can understand from this figure the origin of one of the results of a chronic inflammation, *i.e.*, the formation of a tube abscess.

The tubal wall in chronic inflammation is almost always affected. In most cases there is hypertrophy of the wall, and we see the round-celled infiltration filling the interstices of the muscularis, and also see large circumscribed groups of round cells which resemble lymphomata. The vessels, even up to the peritoneum, are often seen in sections surrounded by a thick circle of round cells.

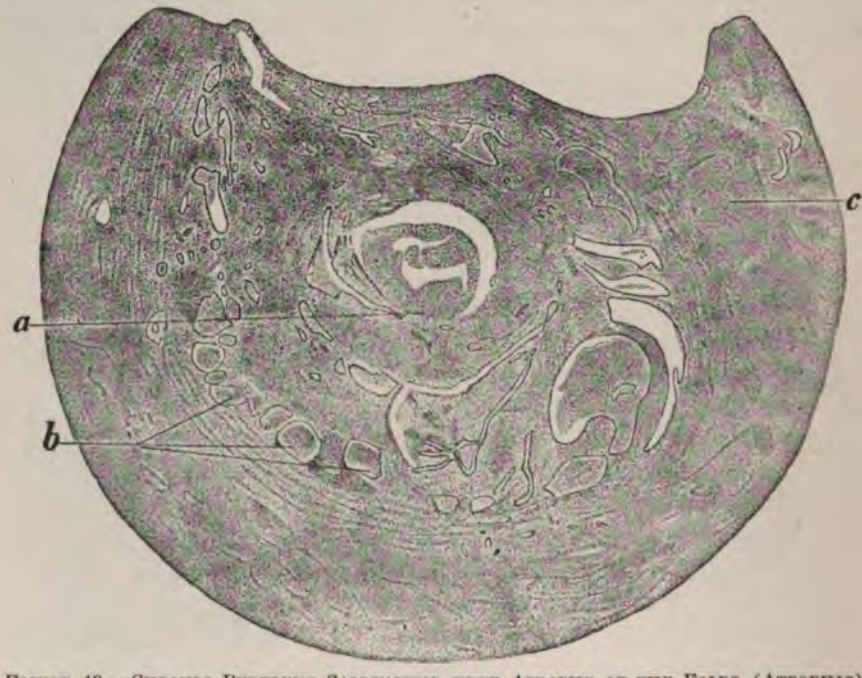


FIGURE 49.—CHRONIC PURULENT SALPINGITIS WITH ATROPHY OF THE FOLDS (ATROPHIC).
a, pus in the tubal canal; *b*, remains of folds; *c*, large collection of pus in the tube wall.

This grouping of round cells in the transition to the chronic stage leads either to the formation of connective tissue, or there is a degeneration of certain parts with the resulting formation of multiple abscesses in the wall. In either case the muscle is gradually destroyed. The only difference is that in the latter case there is a greater fragility of the wall and in the former it is consolidated. In this way we are led directly to the results which chronic inflammation may cause.

If the tendency of the process is toward purulent degeneration we find a *tubal abscess.*

The folds disappear more and more, and through purulent destruction of the wall it becomes decidedly thinned, and perhaps before this the existing septa between the individual sections of the tube are de-

stroyed and there results a genuine tubal abscess after the abdominal and uterine ostia are closed.

How long the epithelium can be retained in such a solitary abscess, in which the pressure of the fluid accumulation is considerable, may be seen in Fig. 51. In this case a tubal abscess almost the size of a fist was present.

The second result of a chronic inflammation is *the formation of new connective tissue.* In such a case the wall always becomes thicker and shows a firm consistence as the result of the connective tissue. The folds become atrophic, the mucous membrance has a stroma of firm

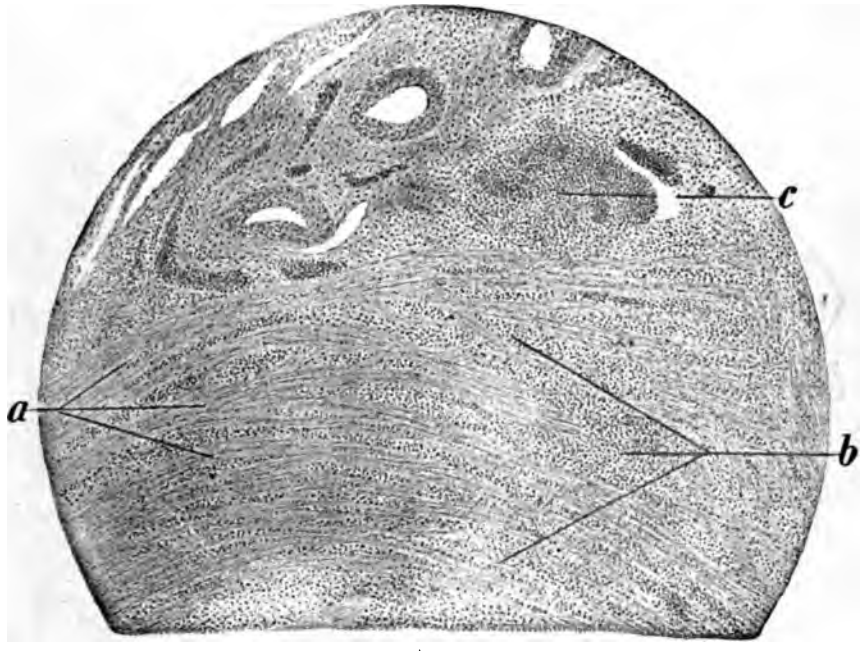


FIGURE 50.—CHRONIC PURULENT SALPINGITIS; ROUND-CELLED INFILTRATION IN THE TUBE WALL *(meso- or myosalpingitis).*

a, muscle of the tube wall; *b*, small-celled infiltration; *c*, round and outlined area of infiltration.

connective tissue, the epithelium may disappear, and there may even result the firm closure of the tubal canal. Such a tube may be thicker than a thumb, and, if no new injuries through adhesion with the abdominal organs take place, may cause the patient no annoyance.

In describing the various anatomical changes which chronic purulent tubal inflammation causes, I have avoided giving a special name to the individual forms.

I should consider it of advantage if others would accept this plan, for all the various titles only cause confusion. In my opinion it is unnecessary, when the above-mentioned formation of adhesions between the

folds simulates glands, to name this microscopical condition salpingitis follicularis, or, what is better, pseudofollicularis. In addition, we hear of salpingitis isthmica nodosa, chronica productiva vegetans, interstitialis disseminata, parenchymatosa chronica, a pachysalpingitis—names which are understood after the above-mentioned description, but which should be considered as unnecessary ballast and thrown overboard.

In the former description we have spoken of and observed only the tubes. As we have often mentioned, however, there occur very early in inflammatory changes adhesions of the tube to neighboring structures, especially to the ovaries, and in this way formations gradually arise where we cannot decide whether we are dealing with the tube alone or with the tube and ovary. We call such formations

FIGURE 51.—TUBAL ABSCESS.

a, pus; *b*, very thin tube wall, with an almost even epithelial lining of the interior; *c*, remaining and atrophic folds.

(*d*) Tubo-ovarian Tumors.

The inflammatory processes which occur on the serous covering of the tubes and ovaries lead to the formation of *delicate, transparent peritoneal adhesions*. These occur either as flat or band-like formations.

Usually there occurs at first a union of the fimbriated end with the ovary, the still open fimbriæ adhering to a corpus luteum and uniting with it, or else the already closed fimbriated extremity is constantly drawn by adhesions closer to the ovary. We often have occasion to operate upon these cases in such a stage in which *the ovary can be*

plainly distinguished from the tube and where the ovary sits upon the tube like a fungus.

We see the membranes gradually extending from all parts of the tube to the ovary, so that with its entire surface it is drawn over to the

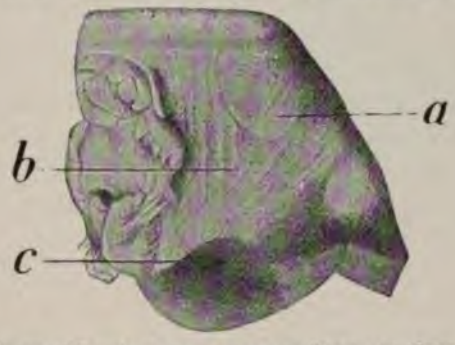


FIGURE 52.—ADHESION BETWEEN TUBE AND OVARY.
a, tube; *b*, transparent membranes between tube and ovary *(c)*.

tube in its entire extent. Both organs may be recognized through the delicate transparent membrane.

In the further course, *the adhesion is always closer*, and out of the delicate transparent membranes are formed firm connective-tissue bands

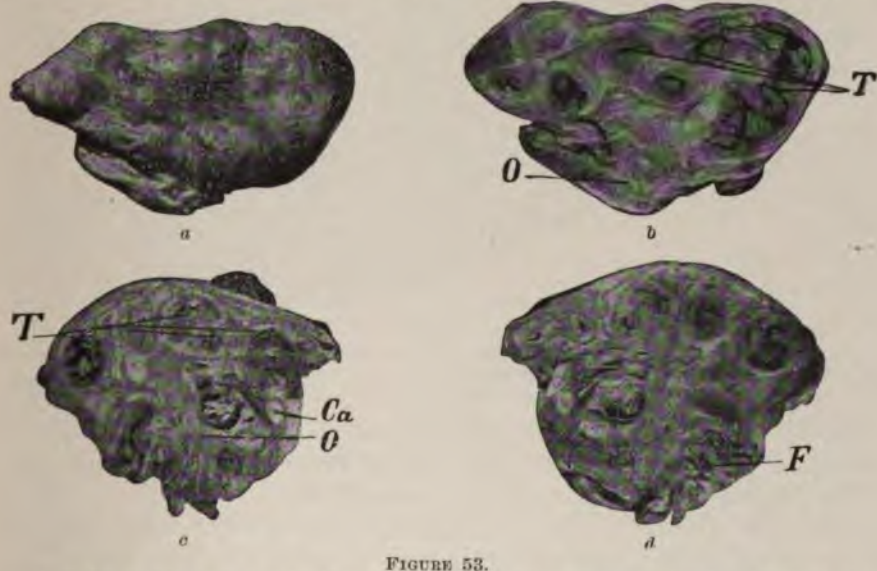


FIGURE 53.
a, tubo-ovarian tumor seen externally; *b*, longitudinal sections through the same (T, tubal twistings; O, ovary); *c* and *d*, longitudinal section through another tubo-ovarian tumor, cut surface opened (T, sections through the twisting tubal canal; O, ovary); *Ca*, corpus albicans; F, closed and retracted fimbriated end.

which cause it to appear as if both organs were one mass, and we then call this condition a tubo-ovarian tumor. Such a tumor is *usually united*

to the posterior surface of the uterus by adhesions, so that in examining we are often unable to clearly define it from the uterus.

The union of both organs does not remain, however, only superficial, so that they may be isolated after the division of the firm membranes, but, *through union of the elements composing these two organs,* there may result actually a single tumor. This may be recognized in longitudinal sections made through the entire tumor, as seen in Fig. 53.

A microscopical section through the uniting membrane makes this condition still more distinct. Even by magnification with an ordinary lens (Fig. 54) it may be seen that we are dealing with a uniform formation. In the early stages we recognize the boundary between the tube and the ovary by a zone of small-celled infiltration. If the process is

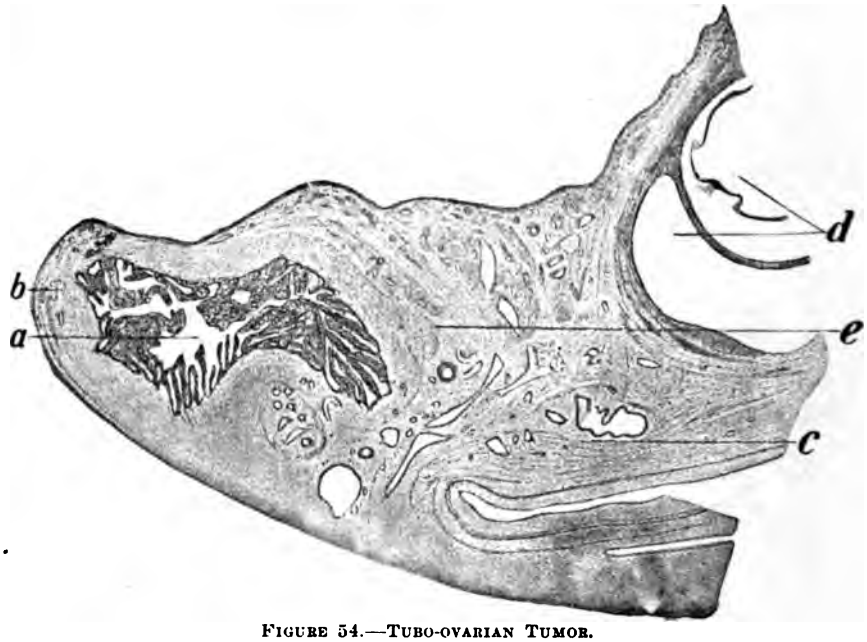


FIGURE 54.—TUBO-OVARIAN TUMOR.

a, section through the ampulla of the tube; *b*, tube wall; *c*, ovarian tissue; *d*, small cysts; *e*, transition of the tube wall to ovary.

more advanced both tissues run into each other by means of a firm connective-tissue union. In this way all further changes which such tubo-ovarian tumors undergo can be easily explained.

If after chronic purulent salpingitis a tubal abscess results, the pus may break through into the ovary and cause a *coexisting ovarian abscess.* Even though no complete abscess is present, but only isolated pus formations in the various parts of the tube, the union of both organs may lead to the penetration of pus into the ovary and the formation of an abscess. Gradually then one large abscess develops. It may happen that the tube goes directly into a corpus luteum, and then a *corpus luteum abscess* may be formed.

When the tubal affection results in healing, both organs are still more firmly united, the structures of both are replaced by connective tissue, and the organs lose their function. It is not my purpose to discuss the union of the affected tubes with other organs, but I should like to mention that a not infrequent adhesion is that *with the vermiform appendix.* The origin of appendicitis from affections of the uterine adnexa is a fact which, in my opinion, has not as yet attracted sufficient attention, even though slight attention has recently been called to this fact.

Finally, it happens that the fimbriated ends of both tubes unite with each other.

(E) Infectious Granuloma.

Under this heading we must include *actinomycosis* in addition to *tuberculosis* and *syphilis.* The former is very rare and usually propagated from other organs. In the pus we find the typical form of the star-shaped fungus. The microscopical changes in syphilis possess no decided criteria so long as we do not know its cause. The few affections observed in syphilis, so far as the tube is concerned, show a chronic productive inflammation.

In *tuberculosis* of the *tube* tubercles form first in the mucous lining and then in the other parts of the wall. At times tubercle bacilli are found in the giant cells, but it is difficult to find them in every case.

The pus formed in this affection is thick and contains cheesy masses. The dilatation of the tubes may be very great. It is remarkable that tuberculosis develops *primarily in the tubes* relatively often. In conjunction with tuberculosis there may occur the well-known "atypical epithelial growths" of Friedländer, which usually remain confined to the mucous membrane, but which may also penetrate the superficial layers of the muscle.

(F) Hypertrophies and Hyperplasias.

Fluctuations in the size of the tubes are very frequent, so that in describing the normal condition we must usually allow a rather wide field of variation. In inflammatory affections there may result decided elongation and thickening of the tube. These may be either one-sided or bilateral. Recently I observed in a double-sided pyosalpinx that the length of the tube from the uterus to its abdominal end was sixteen centimetres. The elongations in myoma of the uterus are still more considerable. In one case operated upon by me the interstitial portion of the tube was twenty-three centimetres long.

The partial hyperplasias lead, as a rule, to the formation of *polyps of the mucous membrane.* These extend into the canal of the tube and may, in some cases, completely close it. We have already discussed such polyps as a cause of the occurrence of tubal gestation. Their micro-

scopical structure shows nothing remarkable. In the polyps the elements of the matrix are reproduced. The vessels are usually increased.

Isolated hyperplasia of the epithelium may occur, in which the stroma of the mucous membrane takes part only as a supporting substance. This causes villous formations such as occur in all hollow organs, and on account of their macroscopical appearance are called *papillomata* (bladder, intestine, ovarian cysts). These are always confined to the mucous membrane.

FIGURE 55.—CARCINOMA OF THE TUBE.

a, carcinomatous bands on the surface of the mucous membrane; *b*, muscle; *c*, carcinomatous masses with an alveolar structure, penetrating deeply into the muscularis.

(G) NEOPLASMS.

As compared with carcinoma, the other new formations are much rarer. Even the carcinomata occur only here and there as primary tumors. They originate, according to our present observations, from the epithelium of the mucous membrane and form epithelial growths of a villous structure. The epithelial strands lie without interstitial

substance, often in irregular groups next to each other, and penetrate the tube wall, whose elements they destroy. This is another characteristic favoring the diagnosis carcinoma. If such epithelial growths are limited to the mucous membrane alone, without showing that characteristic alveolar structure of a carcinoma with which we connect the clinical understanding of malignancy, it lies beyond our power to say with certainty from a microscopical picture whether in such a case we are dealing with a malignant process or not.

Carcinomata with the typical alveolar structure also occur in the tubal wall and the tube lining. The name "papillary carcinoma" of the mucous membrane for changes which do not possess destructive characteristics seems to me to be unfortunately chosen.

I should like to mention that after extrauterine pregnancy a tumor in the tube with destructive tendencies has been described *(chorioma)*.

Rarer than carcinoma is sarcoma of the tube. The majority are round-celled sarcomata.

The benign neoplasms of the tubal wall (myoma, fibroma) occur rarely and show no microscopical peculiarities.

VI. THE OVARIES.

1. NORMAL ANATOMY.

(A) Position and External Form.

Concerning the normal position of the ovary various opinions existed until recently. After a series of examinations which Hammerschlag made in the Berlin Anatomical Institute under the direction of Waldeyer, that position which Waldeyer long ago described has been found to be the normal. We therefore follow the description given by Hammerschlag.

The ovary has a flattened cylindrical form with a convex surface toward the abdominal cavity and a slight concave surface toward the tube. After puberty its length is about 2.5-5 cm., its width is 2 to 3 cm., and its thickness is 1 to 2 cm. Its long axis is almost parallel to that of the body.

The ovary is suspended between the suspensory ligament of the ovary *(running to the cecum and the vermiform appendix on the right side and to the sigmoid flexure of the colon on the left)* and the ovarian ligament (running to the uterus). At its hilus it is fastened to the mesovarium, a fold from the posterior layer of the broad ligament. The hilus edge of the ovary looks forward and outward, the convex edge backward and inward. The wall surface lies close to the lateral wall of the pelvis; the free surface looks toward the pelvic interior and is

covered by the tube and the mesosalpinx. At the places in which the ovary lies during the different periods of age it causes more or less deep impressions in the pelvic wall, *i.e.*, in the peritoneal sac. Between the branches of the hypogastric artery may be considered its typical final position.

Here the ovary lies in a groove caused by its own configuration, the *fossa ovarica,* whose normal boundaries are anteriorly the umbilical artery, the obturator nerve, and posteriorly the uterine artery and the ureter. Waldeyer distinguishes on the lateral pelvic wall from before backward a fossa paravesicalis anterior and posterior, a fossa obturatoria, and a fossa hypogastrica. The ovary occupies as its special region the posterior portion of the fossa obturatoria.

The ovary is united to the uterus by the ovarian ligament, which is attached to the posterior surface below the origin of the tube. The surface of the ovary is not smooth, but shows small elevations and small, sometimes star-shaped depressions. The elevations are caused by the growth of the follicles, which force their way up to the surface, while the depressions are caused by retraction after rupture of the follicles. The ovary has a semi-firm consistence and is of a grayish-white color.

(B) Anatomical Structure.

In the ovary we distinguish two divisions, the vascular layer and the parenchymatous. Unfortunately a certain confusion exists on account of the various names given by various investigators, thus unnecessarily complicating the relatively simple anatomy of the ovary. The classification given above is adopted from the splendid work of Waldeyer on the ovary and ovum, and should be generally accepted on account of its simplicity. We may, however, add, as the external boundary of the parenchymatous, a cortical layer, the albuginea. This cannot be isolated by dissection, but goes gradually over into the parenchyma.

(a) The Vascular Layer.

Through the hilus of the ovary the vessels enter in such number and size that scarcely any other tissue is present between them. The veins in the hilus, mingled with muscle fibres, form a special corpus cavernosum—*bulbus ovarii* (Rouget). A transverse section through this part gives the impression of cavernous tissue. A remarkable corkscrew-like twisting characterizes the ovarian arteries. The arteries enter the ovary in this way and retain this peculiarity in their finer ramifications until they divide into a capillary network. The arteries have strong muscular walls, *the only muscle fibres which exist in the ovary.* In addition to blood vessels, lymph vessels and nerves enter the ovary.

(b) The Parenchymatous Layer.

This layer gives the ovary its characteristic stamp, for it contains the important elements necessary for propagation, namely, the follicles containing the ovum.

(α) The Stroma.

The stroma consists of a firm connective tissue with numerous interlacing fibres and more or less numerous spindle-shaped nucleated cells. Elastic fibres are also found. The nearer we approach the surface the more does the number of nuclei diminish, so that the cortical layer may be said to be a fibrillary connective-tissue boundary of the organ. The surface is covered with peritoneum at the hilus, while the

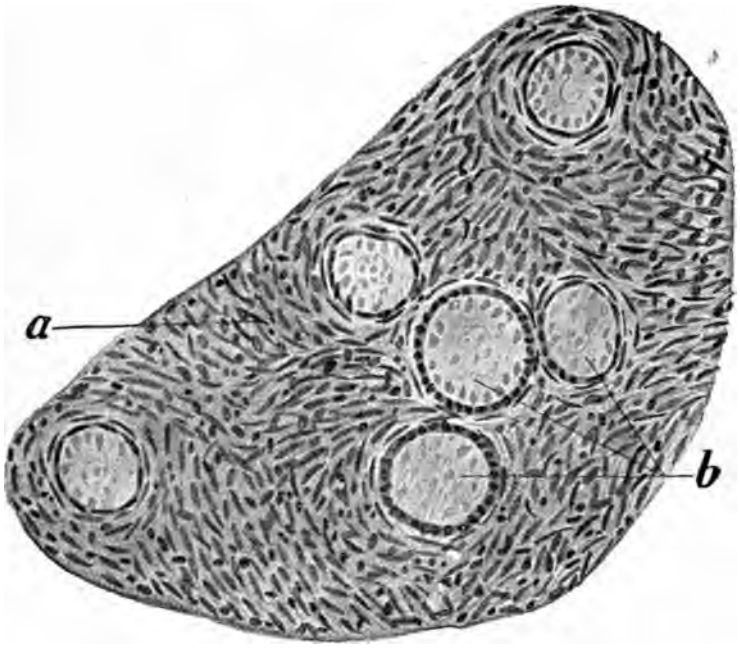


FIGURE 56.—PARENCHYMATOUS LAYER OF THE OVARY, WITH FOLLICLES IN A STATE OF REST.

a, stroma; *b*, follicles (the ova are only faintly evident in a few follicles).

part which projects freely into the abdominal cavity is covered with a more cubical epithelium, the so-called "germinal epithelium," and contains no covering which may be called "corpus serosæ."

The germinal epithelium forms depressions in the tissue only during the period of development of the ovaries. These invaginations of the epithelium are later changed to follicles containing ova.

(β) The Follicle.

The follicles are cyst-like formations which are of various size, according to their state of development (ripening). Their diameter varies between 0.04-1.5 cm.

The small follicles lie in several layers near the surface, the larger ones lie more in the deeper layers. As they grow the ripening follicles again approach the surface, from which they then project.

The smaller follicles may be called

(α) Follicles in a State of Rest.

They surround the ovum with multiple layers of cubical epithelium, which becomes flatter the further advanced the follicle is. Seen in section, strongly magnified, the external layer of the follicle epithelium is like the epithelium of a gland. The internal layer lies in a different plane and the cells are seen from above, so that they appear indistinct and more like squamous epithelium. In the middle of the follicle lies the ovum.

The ripening of the follicle is shown by the formation of vacuoles in that part of the epithelium lying near the surface of the ovary. The resulting space, becoming continually larger, is filled with a clear fluid, the *liquor folliculi*. It contains pseudomucin. At the same time an increase in the vessels is observed at the periphery, as the beginning of a special connective-tissue cover. This stage of development, in which the growing egg causes an active proliferation of the epithelium of the follicle with formation of the follicle fluid, is given an especial name, the Graafian or vesicular follicle (folliculus vesiculosus).

(β) The Graafian Follicle.

The Graafian follicle is surrounded by a connective-tissue wall *(theca folliculi)* in which we distinguish an external firm layer poor in cells and an internal layer rich in cells and containing vessels *(tunica fibrosa and propria)*. I would call attention to the fact that these two layers cannot always be distinctly outlined in the microscopical picture.

The following follicle epithelium surrounds the liquor folliculi in multiple layers *(membrana granulosa)*, the outermost cells being of cubical form, while on the inner surface they are flattened.

At that part of the follicle where the ovum is found, generally opposite the surface, there is formed a considerable grouping of epithelial cells of the follicle *(cumulus or discus proligerus)*. Toward the liquor folliculi the ovum is marked off by a less dense, and in parts a single, layer of epithelium. The ovum possesses an external membrane *(zona pellucida)*. This shows a radial striation and surrounds the protoplasm *(yolk)* in which the nucleus *(germinal vesicle)* and the nucleolus *(germinal spot)* lie.

(c) The Further Course of the Ripe Follicle.

When the ovum has completely ripened the follicle projects in part above the surface of the ovary, and at a certain time bursts and dis-

charges the liquor folliculi and the ovum. At that point at which this rupture takes place the wall is decidedly thinned.

At the time of bursting an extravasation of blood into the cavity of the follicle takes place. Later certain changes in the way of proliferation occur which lead to the formation of the so-called *corpus luteum.*

These changes are quantitatively greater if pregnancy takes place through fecundation of the expelled ovum *(corpus luteum verum)*; less decided if the ovum is not fecundated *(corpus luteum spurium).* The character of the change is the same in both cases.

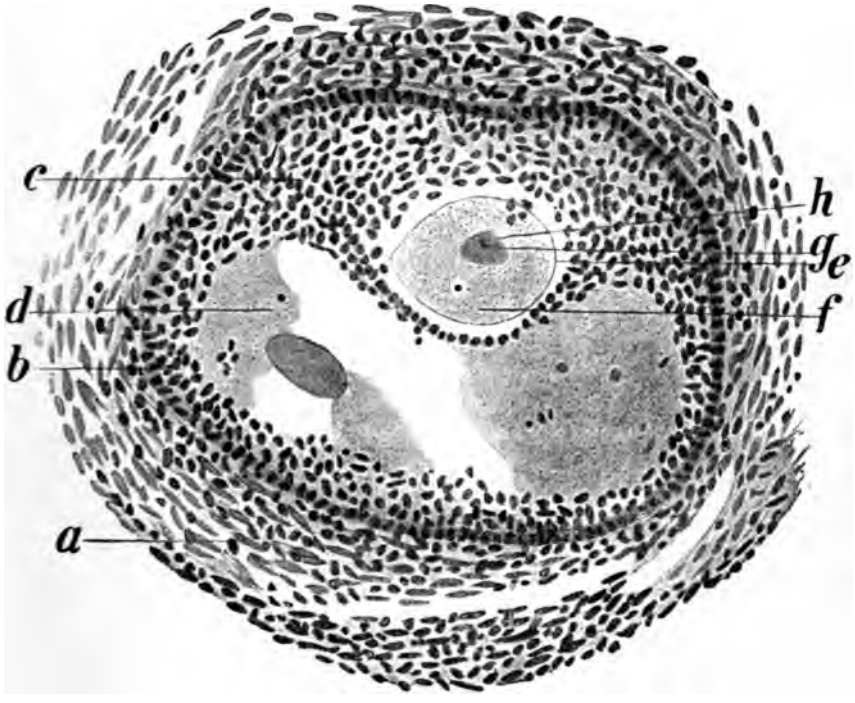


FIGURE 57.—GRAAFIAN FOLLICLE.

a, theca folliculi; *b*, membrana granulosa; *c*, cumulus or discus proligerus; *d*, liquor folliculi; *e*, zona pellucida; *f*, yolk; *g*, nucleus; *h*, nucleolus.

(α) The Corpus Luteum.

After expulsion of the ovum from the follicle the lacerated area unites quickly. From the wall comes active growth and formation of new vessels. These send branches into the membrana granulosa and carry to these cells new nutritious material, so that a decided enlargement and an increase in the number of these cells results. These cells take on a character resembling the decidua cells, and line the wall in numerous overlying layers. These cells project more or less into the interior filled with blood, so that a ruffle-like lining is formed.

We call these cells, which frequently contain pigment and which

give the corpus luteum its characteristic stamp, *lutein* cells. Whether these lutein cells originate from the follicle epithelium, or whether they are connective-tissue cells furnished by the theca interna, is still an open question. I hold to the view that they originate from the follicle epithelium (Sobotta).

As a result of the pigment deposited in the lutein cells and the blood poured into the interior of the follicle, the latter has a yellow appearance, wherefore it is called "the yellow body." After a time

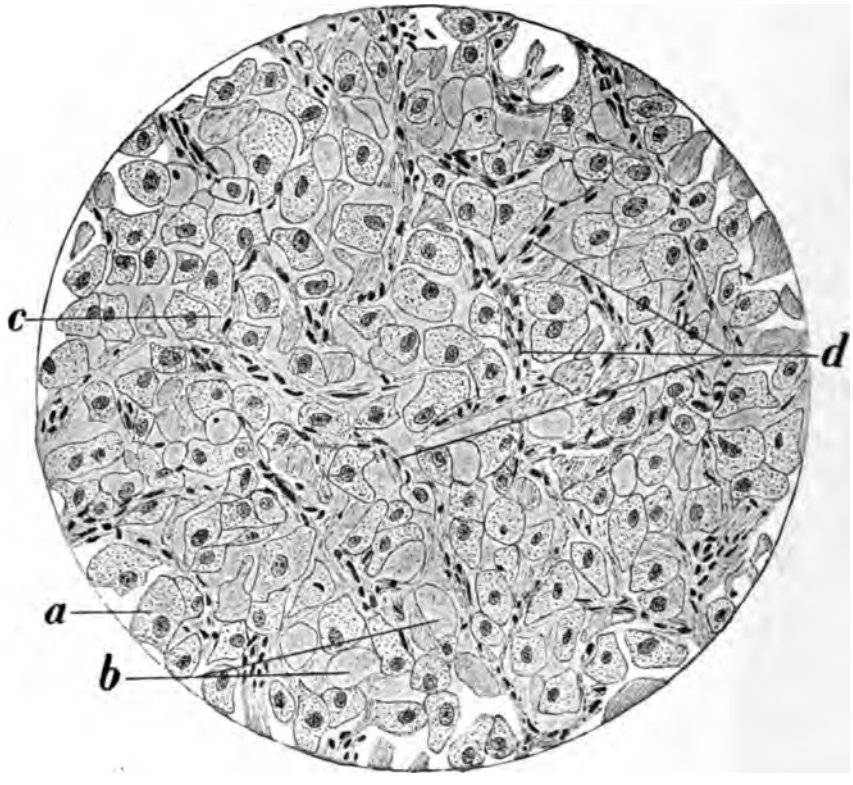


FIGURE 58.—FROM THE WALL OF A CORPUS LUTEUM.

a, lutein cells; *b*, spaces resulting from loss of lutein cells (artificially produced); *c*, lymph spaces between lutein cells; *d*, capillaries with endothelium and connective tissue.

the growth of the lutein cells ceases and the blood coagulates and is organized, the lutein cells gradually disappear, an active production of connective tissue displaces them from the circumference, so that in this way the entire interior is filled with connective tissue and we have a

(β) Corpus Albicans.

This represents the end stage of the follicle after it has completed its function. This may be compared to the end stage of a chronic inflam-

mation, leading not to restitution, but to connective-tissue formation. In a section through an ovary the corpora albicantia are outlined as white, shiny, irregularly rounded or stellar formations. Every rupture of a follicle leaves behind on the surface of an ovary a scarred depression. In this way gradually numerous depressions are formed, and between them prominences which occasionally resemble the convolutions on the surface of the brain, as I have observed in a remarkable case of this sort (ovarium gyratum).

(c) The Ovary during Menstruation and Pregnancy.

As a result of the congestion of the genitalia during menstruation the ovarian vessels are also filled with blood. As a rule, there is no extravasation of blood into the ovarian tissue. I cannot enter into the physiological relation between ovulation (the ripening and expulsion of the ova from the follicle) and menstruation. I should like to mention that, according to recent investigations on this subject, the opinion that menstruation is dependent on ovulation is becoming stronger.

In pregnancy the ovary which expelled the fecundated egg or ovum becomes larger than the ovary of the other side, through the formation of the corpus luteum. The other changes in the ovary in pregnancy are limited to an enormous enlargement of the vessels. No special changes in the parenchyma or epithelium of the ovary occur. It deserves no further mention that, of course, with the growth of the uterus during the progress of pregnancy the ovaries change their position and ascend into the false pelvis.

(d) Senile Atrophy of the Ovary.

When menstruation ceases *(climacterium)* an increased formation of connective tissue results, which leads to atrophy of the follicles, to a thickening of the albuginea, and to a shrinking of the entire ovary.

2. PATHOLOGICAL ANATOMY.

(a) Ovarian Gestation.

Even though ovarian pregnancies are of little practical importance compared with tubal gestations, it must be mentioned that an ovum may also develop on the surface of an ovary. It has been stated that the fibrous layers of the albuginea have been seen directly continuous with the fibrous covering of the fetal sac. It has also been stated that an ovum may develop within a follicle.

(B) Disturbances of Circulation, Hyperemia.

As in the uterus, disturbances of circulation in the ovary are generally the result of infectious diseases. There results either bleeding into the follicle and the corpora lutea or into the interstitial tissue. The hemorrhages may in certain cases become so pronounced that the larger portion of the interstitial tissue is destroyed and a hematoma of the ovary results. Through rupture of such a space filled with blood, hemorrhages which endanger life may occur into the free abdominal cavity.

Among other causes which lead to such bleedings may be mentioned those injuries which the individual may meet with during menstruation (trauma).

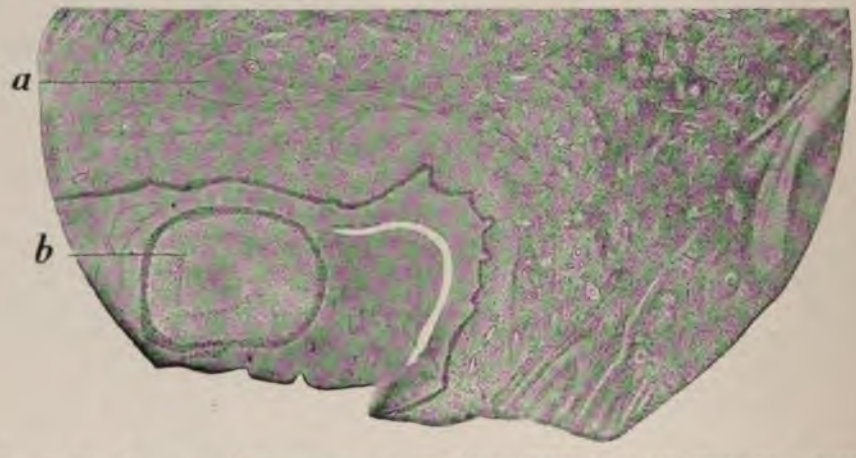


Figure 59.—Enormous Hypertrophy of the Blood Vessels in an Ovary in a Case of Myoma of the Uterus.

a, connective-tissue degeneration in the stroma; *b*, cystic formation in a follicle.

Hyperemia with considerable new formation of vessels may be observed, aside from inflammatory infections, especially in neoplasms of the uterus, if these have reached a considerable size, and particularly *in large myomata*. There results an enlargement of the entire ovary, its individual elements becoming hypertrophic through the increased supply of blood. That condition is illustrated in Fig. 59, the section being taken from such an ovary associated with a very large myoma of the uterus.

(C) Inflammation.

The inflammations of the ovary are of so little practical importance as compared with neoplasms that we will confine ourselves to a discussion of the most essential points only.

(α) Interstitial Oöphoritis.

In the interstitial form we distinguish a chronic and an acute stage. The acute inflammation is chiefly caused by a *septic or a gonorrheal* infection, and causes a marked small-celled infiltration of the interstitial tissue with simultaneous hyperemia and increase of the vessels.

Extravasation of blood into the tissue may result, and if at the same time there is an entrance of pyogenic bacteria, formation of pus takes place. The suppuration involves either the entire tissue, the pus changing the entire ovary into a large abscess cavity *(ovarian abscess)* by breaking through the walls of the follicle, or else the suppuration is confined to individual parts. In this way there results not infrequently a suppuration of the corpora lutea and the formation of *corpus-luteum abscesses.*

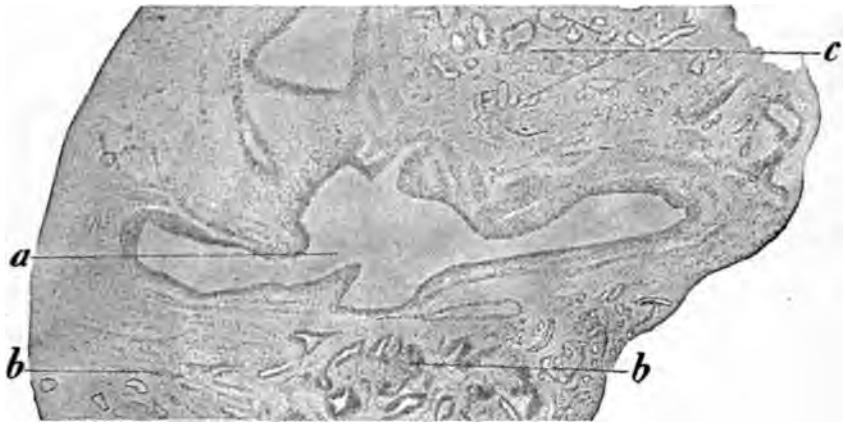


FIGURE 60.—INTERSTITIAL OOPHORITIS.

a, section through a large vein; *b*, small-celled infiltration; *c*, newly-formed vessels.

The characteristic of these abscesses is that we find in them a wall consisting of lutein cells. Macroscopically we see in large abscesses of this sort, on section, *wavy elevations of the inner wall.* This form we have learned in discussing the normal anatomy of the corpora lutea.

In the *chronic* form there results the formation of connective tissue with retraction. The follicles are mostly destroyed and the stroma shows, in place of the numerous cell elements, fibrous connective tissue. The epithelium of the surface is preserved longest in such a condition. When this is destroyed it may, however, still be observed in the folds or sinuses which have been caused by retraction.

I do not desire to consider as a separate division the so-called "Follicular Oöphoritis," but refer to the chapter on small cystic degeneration.

(β) Perioöphoritis.

In connection with an oöphoritis there frequently occurs a perioöphoritis in which inflammatory deposits are formed on the surface of

the ovary, leading to adhesion with neighboring organs, especially the tube, uterus, and intestines. Such adhesions are more frequently formed *secondarily,* as a result of tubal affections, as we have already seen. The adhesions lead to the formation of the tubal tumors already mentioned. The germinal epithelium of the surface is early destroyed by this process. Perioöphoritis may also secondarily give rise to an oöphoritis.

(D) Infectious Granuloma.

The syphilitic affections of the ovary are as yet little known, so that we possess no positive characteristics for their microscopical determination.

Tuberculosis frequently occurs *secondarily,* but rarely primarily, in the ovary. As a rule, we see tubercles with giant cells in the interstitial tissue. At times such tubercular masses are found in the wall of the cysts or in the walls of a corpus luteum. The presence of tubercle bacilli can rarely be proven.

(E) Parasites.

The repeated observation of echinococci in the ovary recently leads me to call attention to their occurrence. The positive microscopic proof that the echinococcus affection has taken its origin from the ovary can only be furnished by finding ovarian tissue in the wall of the sacs. Such early stages, however, have not yet been observed. Proof that we are dealing with an echinococcus cyst of the ovary can only be furnished, according to B. S. Schultze, by showing the characteristic position of an ovarian tumor in its relation to the tubes and mesosalpinx.

(F) Small Cystic Degeneration.

The transition from inflammatory processes in the ovary to neoplasms is furnished by retention cysts. These originate, as a rule, in consequence of chronic inflammatory changes. Through the resulting hyperemia there occurs a serous exudation from the vessels of the theca interna, and an effusion of serous fluid into the follicle. A portion of the epithelium of the follicle disappears and is replaced by fluid. The lining of the cyst wall consists of cuboidal epithelium. If the process is far advanced the greater portion of the interstitial tissue may be replaced by cysts. In the early stages the remaining interstitial tissue is infiltrated with small cells. The cysts, as a rule, attain the size of a ripe Graafian follicle; still larger ones have been observed. In the latter the epithelium lining the wall is destroyed by pressure of the fluid. The cyst fluid is usually cloudy from degeneration of the epithelial cells. It is therefore seen that in these retention cysts the epi-

thelium plays only a passive rôle. The contents of these cysts, in contrast to those of true neoplasms, include pseudomucin.

(G) Neoplasms.

By neoplasms of the ovary we understand those tumors which do not result from inflammatory causes, but which are the result of irritations whose nature we do not yet comprehend. Whether we are dealing with

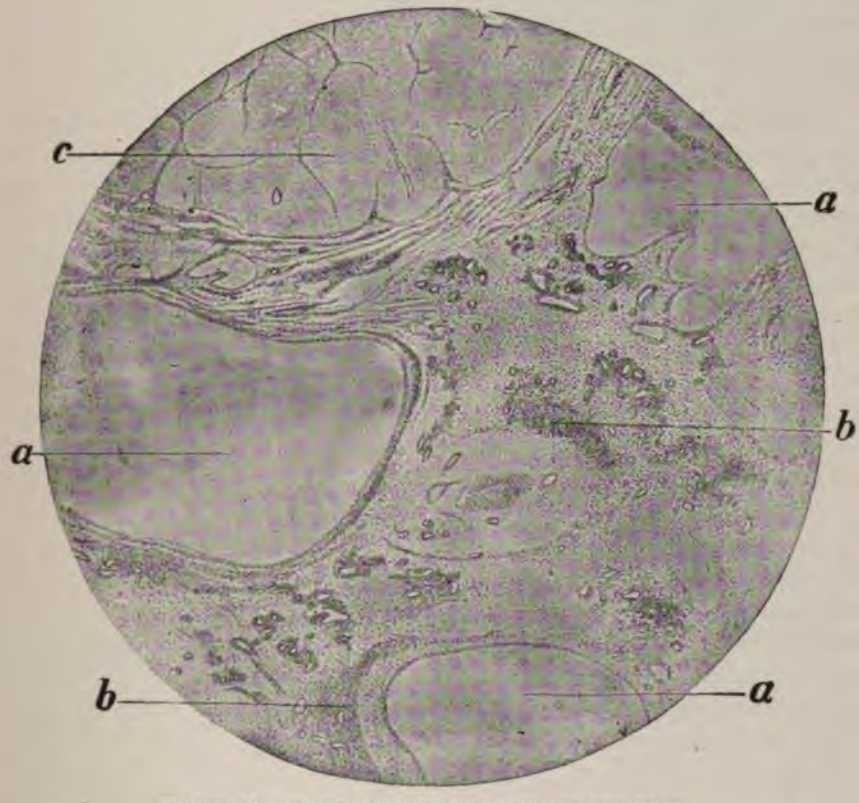


Figure 61.—Microcystic Degeneration of the Ovary.

a, follicles which have undergone microcystic degeneration; *b*, small-celled infiltration; *c*, corpus albicans.

a further growth of *cells dating from the embryonal period*, or whether some *form of parasite* is to be considered, cannot be decided in the light of our present knowledge.

The tendency to the formation of cysts is characteristic of tumors of the ovary. As a matter of fact, solid ovarian tumors are in the background compared with cystic. For the classification of these growths in an anatomical work like this, only anatomical and genetic points of view are considered.

We therefore distinguish two main forms: those which take their origin from the epithelium, and those which originate from the connective tissue. Some authors desire to divide these epithelial neoplasms into groups, according as they originate from the various forms of epithelium found in the ovary. But this does not simplify matters. In addition such a division is unnecessary, since the follicle epithelium originates from the germinal epithelium and genetically is the same. The present division, found in text books, into solid and cystic tumors may be clinically correct, but in an anatomical description would lead to repetitions.

1. Epithelial Neoplasms.

(α) Surface Papilloma.

Surface papillomata are rare as compared with cystic formations. The germinal epithelium in these growths proliferates and forms nodular elevations above the surface. The ovary acquires in this way an irregular appearance, and cauliflower-like formations may result from further growth. In this way there are formed in these elevations depressions of epithelium, such as occur in pointed condylomata, so that the various forms have a very irregular appearance. Connective tissue gradually makes its way into the originally purely epithelial elevations, but it is characteristic that the growth remains confined to the surface, and that deeper depressions of the epithelium into the ovarian stroma do not occur. In that way these papillomata resemble the epitheliomata of the other organs.

(β) Follicle Cysts.

In contrast to the retention cysts due to inflammatory causes, as we have already learned, there may also occur genuine cystic neoplasms which may cause a decided enlargement of the ovary. As a rule, a large number of follicles undergo cystic degeneration, so that in one section through the ovary we obtain a picture resembling a honeycomb with various large cells. By union of several cyst walls and their subsequent disappearance, one large cyst may result. The follicle epithelium may be replaced by cylindrical cells. These line the wall and are preserved even when the neoplasm increases greatly in extent, and they continue to produce the cyst contents. The ova which are present in the follicles are early destroyed. Cystic degeneration may occur in a corpus luteum just as in a follicle, and very interesting formations result, to which recently attention has repeatedly been called.

(γ) Corpus-Luteum Cysts.

The proliferation of the lutein cells which takes place after the ovum has been expelled from the Graafian follicle, and which normally terminates after a certain period and then gives way to connective-tissue contraction, may continue, under circumstances which we do not yet understand, and may lead to the formation of cysts of the corpus

luteum. These, as a rule, do not attain any considerable size, so that a growth the size of a fist is rare.

Macroscopically we can recognize the irregular wavy surface of the inner wall of this cyst. In section the wall is seen to be of considerable thickness, and the wavy elevations extending toward the cyst interior look like those found in a corpus luteum. This alone, however, is not sufficient for diagnosing such a cyst; microscopical examination of the wall is absolutely necessary.

We then see that the wall of a corpus-luteum cyst has a very characteristic structure. We distinguish three layers, an external, a middle, and an internal. The latter goes over with a sharp demarkation into the viscous yellow contents, in which no special formed elements can be distinguished. In stained sections these three layers may be macro-

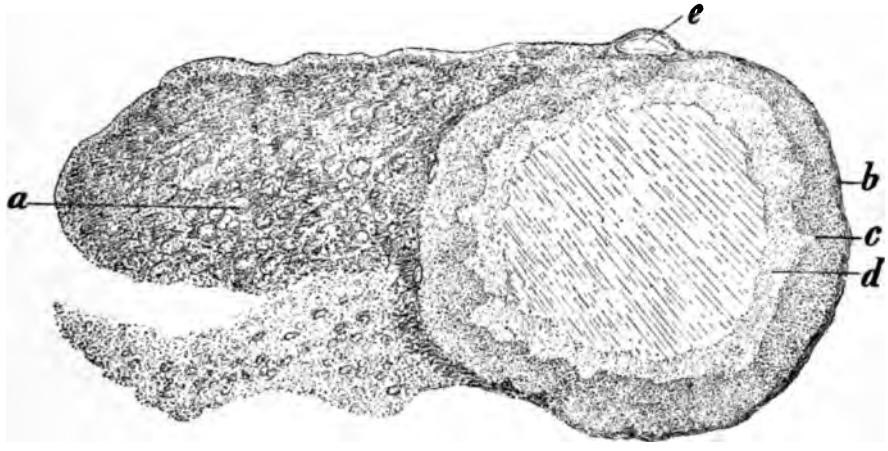


FIGURE 62.—CORPUS-LUTEUM CYST *(enlarged three times)*.

a, ovarian tissue; *b*, external layer of the cyst; *c*, middle layer; *d*, inner layer; *e*, small follicle cyst.

scopically recognized by the varying intensity of the stain. The external layer is most deeply stained, the middle less, and the internal layer scarcely at all. These cysts are usually found at one pole of the ovary.

The external layer has a connective-tissue stroma, in which numerous vessels, mostly arteries and veins, run in a circular direction. Around the vessels at many points are seen groups of round cells. From these main vessels numerous branches pass in a perpendicular direction into the middle layer, in which they dissolve into a capillary network. *The middle layer gives the cyst wall its characteristic stamp*, because the well-known large lutein cells lie between the vessels and the capillaries. They occupy almost the entire space between the vessels, and are only interrupted in the course of the vessels by groups of round cells, which follow the course of the vessels, so that occasionally only these round cells are seen and the underlying capillaries cannot be distinguished. The

more we approach the inner layer the less distinct is the contour of the lutein cells. In part they are without nuclei. The inner layer shows only the transition of the cellular elements of the cyst contents, which are undergoing regressive changes.

The contents show large lutein cells in a state of dissolution lying in a delicate connective-tissue network forced apart by homogeneous

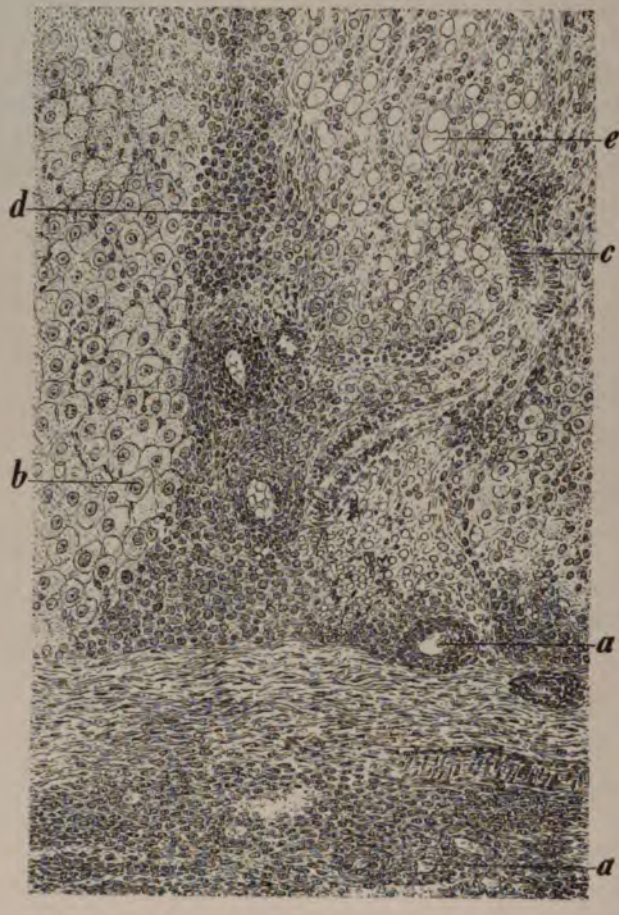


FIGURE 63.—FROM THE WALL OF A CORPUS-LUTEUM CYST *(highly magnified)*.

a, vessels of the outer layer of the cyst wall; *b*, lutein cells of the middle layer; *c*, capillaries cut longitudinally; *d*, grouping of round cells; *e*, spaces resulting from the artificial removal of the lutein cells.

fluid. At certain points are seen strands of wavy connective tissue extending toward the cyst contents.

The inner layer is in most cases not lined off from the cyst contents by epithelium, as is the case in real cystomata of the ovary. This absence of an epithelial lining of the inner wall is considered by some authors to be the principal characteristic of corpus-luteum cysts.

Recently corpus-luteum cysts have been described in which such an epithelial lining was present. According to my investigation, this epithelial layer, if it is present at all, is destroyed very early. This can be explained by the fact that this epithelium plays only a passive rôle, and is destroyed through the pressure of the increasing fluid contents.

The main rôle in the origin of these cysts is played by the lutein cells, which are in a stage of abnormal proliferation and degeneration. In this way the degenerating cells and those forming the cyst contents are continually regenerated. The cyst contents obtain their peculiar color from the pigment which the lutein cells contain.

It may be seen from these conditions that these cysts (so far as the lutein cells are derived from the follicle epithelium) are justly reckoned with the genuine epithelial neoplasms of the ovary. It is evident, on the other hand, that cysts cannot be called corpus-luteum cysts simply because they have no epithelial lining to the wall.

For their diagnosis it is necessary to show the presence of lutein cells in the middle layer of the wall. It is possible that in the later stages these lutein cells may be destroyed, and, after this, enlargement of the cyst could no longer continue. Then only the wrinkling of the wall would remain as a characteristic. It must be mentioned that even in large cysts of this sort lutein cells have been found, and that, on the other hand, a wrinkling of the inner wall may occur in ordinary cystomata.

(*d*) Cystomata or Cystadenomata of the Ovary.

The cystomata are the most frequent form of tumor found in the ovary. They are either uni- or bilateral, and may reach a very enormous size. The cystomata, in contrast to follicle cysts, probably develop from *displaced epithelial cells.* For this reason they must be reckoned among the glandular neoplasms, the adenomata, whose epithelial cells are able to produce large quantities of fluid. It would be anatomically correct, therefore, to consider these tumors as cystadenomata. According as the inner wall is smooth or lined with polypoid growths we distinguish *simple cystadenoma* from *papillary cystadenoma.*

(a) Simple Cystadenoma.

Simple cystomata are either uni- or multilocular—*i.e.,* they form either one large cystic cavity or contain in addition to one large main cyst a series of smaller accessory cysts. Through union of the various walls and the disappearance of the latter, a simple cyst may result from a multilocular. The wall is more or less thick according to the degree of dilatation of the cyst. The cyst wall contains a connective-tissue basis in which are very large blood vessels, especially veins. In parts we see a small-celled infiltration. In long-standing cysts the wall may contain much fibrillary connective tissue.

The inner wall is lined with cylindrical epithelium which continually produces fluid. At times the cylindrical epithelium is changed to the ciliated form. In spite of the dilatation of the cysts the epithelium which forms an essential part of them is preserved. The external surface of the cysts occasionally shows the presence of germinal epithelium still preserved.

The contents of the cysts consist of a somewhat sticky fluid, usually clear as water. At times the fluid is cloudy and may be brownish red from admixture of blood. The most important chemical ingredient of the fluid is pseudomucin. In the smaller cysts ovarian tissue is sometimes found in the wall.

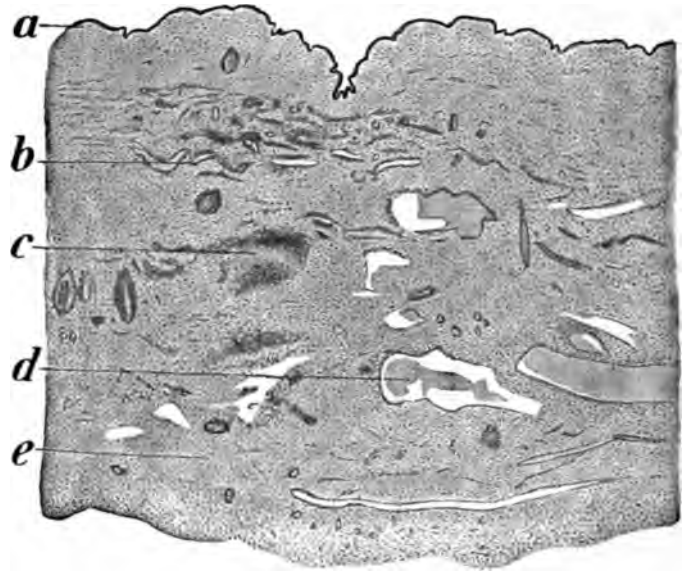


FIGURE 64.—SECTIONS THROUGH THE WALL OF A SIMPLE CYSTADENOMA OF THE OVARY.
a, cylindrical epithelium lining the inner wall; *b*, vessels; *c*, groups of round cells; *d*, dilated lymph vessel with colloid contents; *e*, connective-tissue stroma.

The true *adenomata,* consisting exclusively of glandular depressions and epithelial inclusions without the formation of cysts, rarely occur in the ovary. When they do they usually form transition stages to carcinomata and will be considered under that heading.

(b) Papillary Cystadenoma.

Frequently the inner lining of a cystoma is not smooth, but shows villous projections which extend into the cavity in dendritic ramifications. These projections are made up partly of connective tissue extending from the wall of the cyst, or else are formed of epithelium, as is the case in surface papillomata. Macroscopically the inner surface ap-

pears to be covered with larger or smaller nodular structures, of which some have a smooth and others an irregular surface. At any rate, a very energetic epithelial growth occurs in these formations. This is shown by the fact that the epithelial growth is not confined to the inner surface alone, but that epithelial masses which preserve a glandular form *penetrate to the wall, extend up to the peritoneum,* and may give the outer surface of the cyst an irregular appearance (proliferating glandular cystadenoma, Waldeyer).

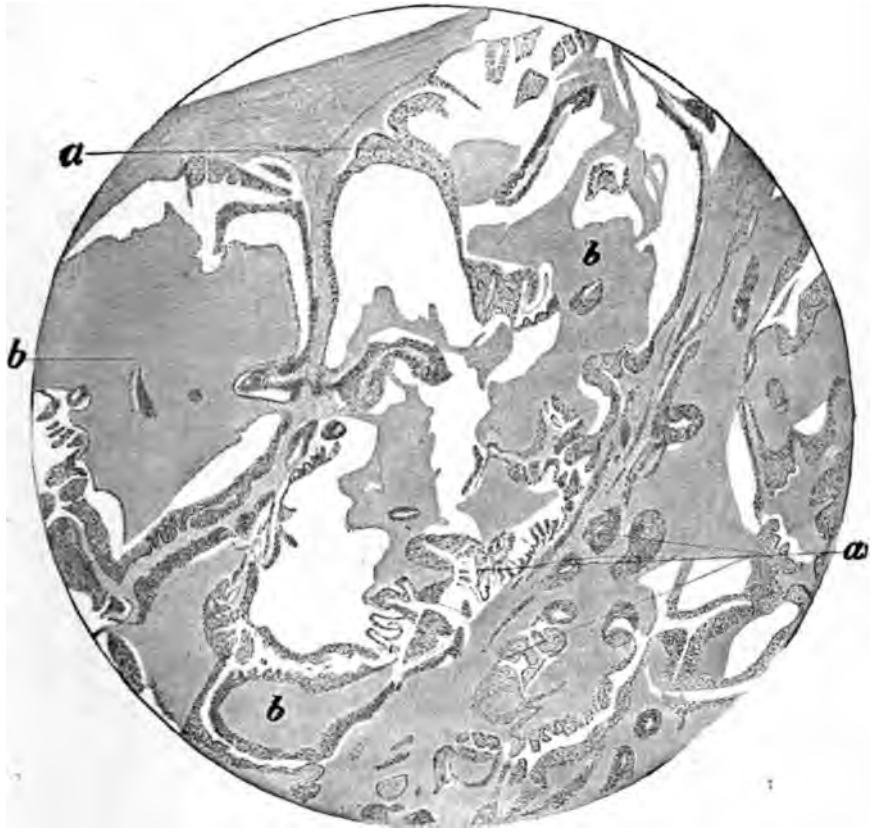


FIGURE 65.—PROLIFERATING GLANDULAR COLLOID CYSTADENOMA.
a, papillary excrescences consisting of cylindrical epithelium; *b*, colloid masses.

In this event these formations stand on the border line between benign and malignant growths. *So long as the outer cyst wall is not penetrated* no metastases can be formed in other organs. If these tumors are removed at this stage healing usually follows without a recurrence. *If, however, the outer wall is perforated,* nodules are formed on the omentum and the neighboring intestine. At any rate, it seems to be more the further growth of epithelial formations than a real occurrence of metastases. As soon as the surface is broken through the tumor unites with the neighboring organs and a continued growth takes place. Even

such advanced cases do not have a necessarily unfavorable prognosis unless operated upon too late and after a real carcinoma is present.

The contents of these papillomata are the same as those of the simple cystomata. Frequently a colloid degeneration of the tissue takes place, so that the contents are mixed with a tenacious colloid mass. In the usually homogeneous colloid substances we see now and then the remnants of epithelial cells. A pseudomyxomatous formation may result in the presence of an enormous quantity of a yellow and very tenacious fluid. I have recently observed such a case in which the ovarian cyst had ruptured, and where the tenacious contents were poured out into the

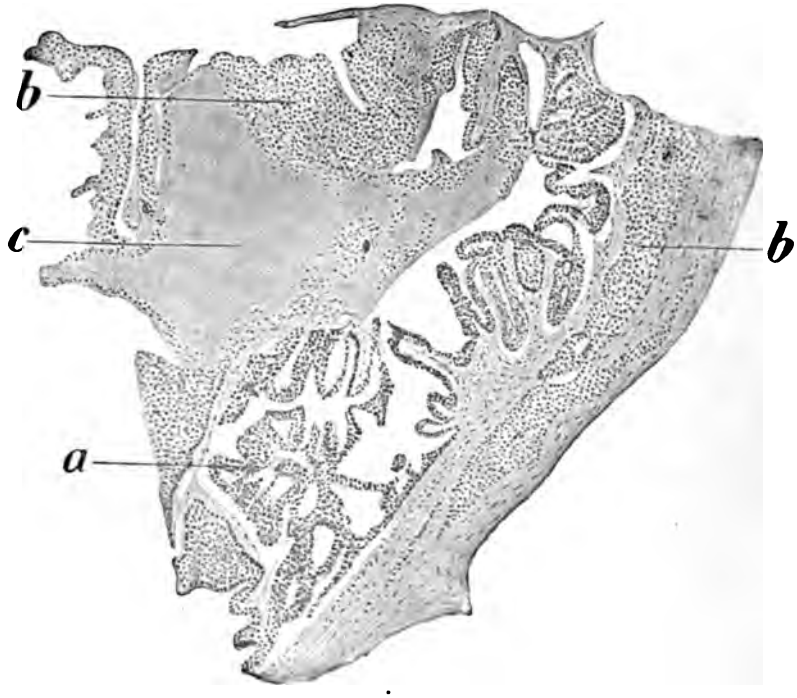


FIGURE 66.—CYSTADENOMA GLANDULARE PROLIFERUM COLLOIDES.

a, formation of epithelial growths; *b*, solid atypical epithelial growths; *c*, colloid masses with cell remnants.

abdominal cavity, with the result that the *parietal peritoneum had undergone pseudomyxomatous degeneration*. After operation, convalescence without reaction. The rupture caused no symptoms.

Among other changes of the cyst wall and contents *hemorrhages* and *calcification* must be mentioned, for these are not rare occurrences. Hemorrhages in the wall and into the interior of a cyst result, as a rule, from torsion of the pedicle, and may be so severe as to endanger life. The contents, especially of small cysts, at times show calcium formations, and calcification of the wall may result, either over a large area or only as granular deposits.

(ε) Carcinoma of the Ovary.

Carcinoma of the ovary occurs either as a solid tumor or as a degeneration of an ovarian cystoma. In the latter case there is formed a mixed tumor, adenoma and carcinoma: cystic adenocarcinoma or cystadenoma carcinomatodes.

A typical alveolar carcinoma infiltrates the ovary with cords of epithelial cells which in their form and structure are not unlike tubal carcinomata. At any rate, as a rule the type of cylindrical-celled carcinoma

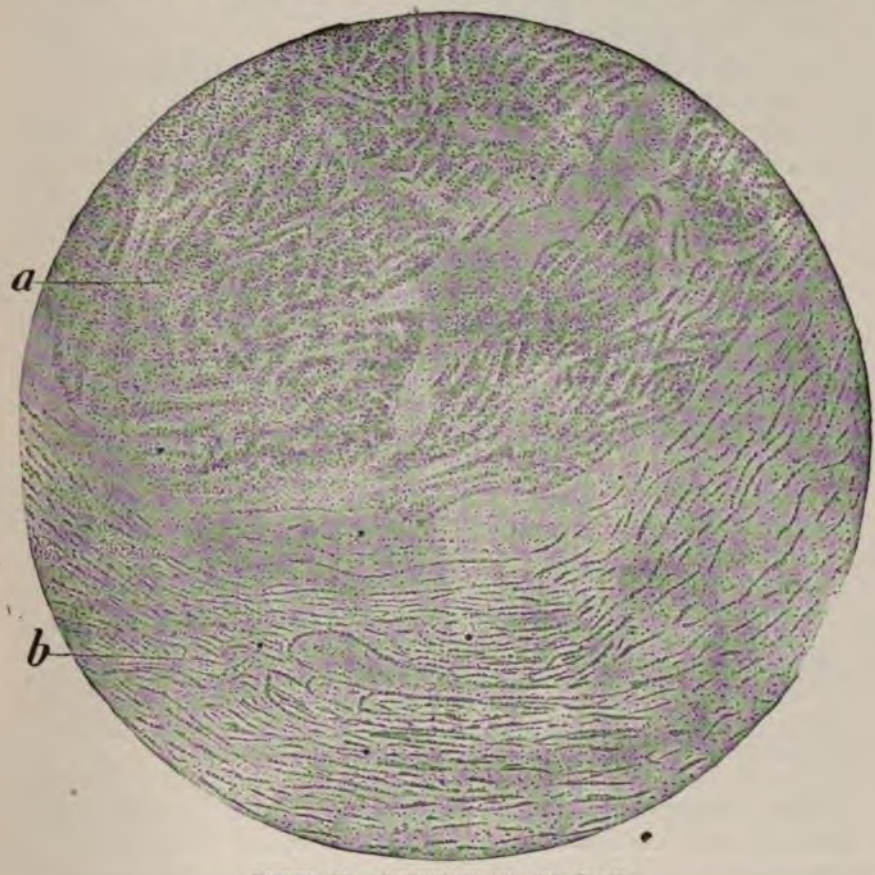


FIGURE 67.—CARCINOMA OF THE OVARY.

a, cancer cells in large round groups; *b*, cancer cells in strand-like arrangement (in lymph spaces?), between them small-celled infiltration.

is preserved. In Fig. 67 may be seen the cells lying partly in nests, partly in single rows, infiltrating the tissue in strands, as if they were lying in preformed channels (lymph spaces?).

The carcinomata cause a rapid enlargement of the ovaries and give them an uneven surface by their irregular growth. The malignancy of ovarian carcinomata does not seem to be so great in the early stages as is the case in carcinoma of the uterus, for metastases do not form so

quickly. The first metastases are usually formed on the peritoneum and in the omentum through the lymph and blood channels.

Cystadenomata *whose growth causes perforations of the wall* not infrequently undergo carcinomatous degeneration. We see, in addition to the papillary and glandular growths infiltrating the wall, typical cancer nests. The glandular formations are partly lined with several layers of cylindrical epithelium. Between the carcinomatous alveoli are found spaces filled with round cells.

Since not only the glandular formations perforating the wall become carcinomatous, but also the papillary outgrowths, we frequently find free carcinomatous masses in the cyst contents. It is important to recognize this fact, for if carcinomatous degeneration is suspected *such a papilloma should not be punctured before extirpation,* for then carcinomatous masses entering the peritoneal cavity may easily cause a transplantation of carcinoma cells to take place.

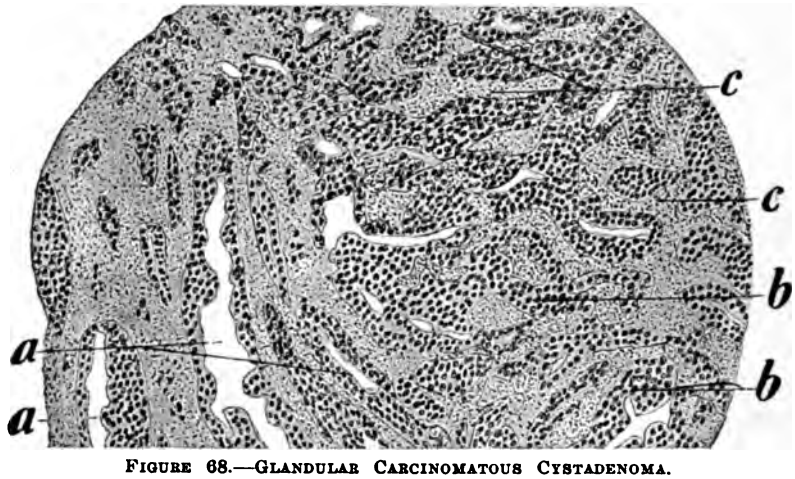


FIGURE 68.—GLANDULAR CARCINOMATOUS CYSTADENOMA.

a, glanular formations, partly lined with stratified epithelium *(b)*; *c*, small-celled infiltration.

Such tumors should always be removed *in toto.* It should also be mentioned that carcinomata of the ovary are usually bilateral. Ovarian carcinomata of long standing form adhesions with the peritoneum, and we have a carcinomatous peritonitis with bloody ascites. While the carcinomatous degeneration of a cystadenoma causes the formation of cylindrical-celled cancers, squamous epithelial carcinomata have been observed in dermoid cysts, originating from the squamous epithelium present in them.

2. CONNECTIVE-TISSUE NEOPLASMS.

(α) Fibroma.

Compared with the epithelial neoplasms, those of the connective tissue are rarely observed. Fibromata of the ovary lead to a disappearance of

the ovarian tissue, which is replaced by fibrous connective tissue. In this way the ovary becomes four or five times its normal size, and even larger growths occur. The external form of the ovary is usually preserved. Such fibromatous enlargements of the ovary may be most often observed with large uterine myomata. Fibrous polyps which rest on the surface of the ovary have been described. At times adenomatous and cystic degenerations of these fibromata take place.

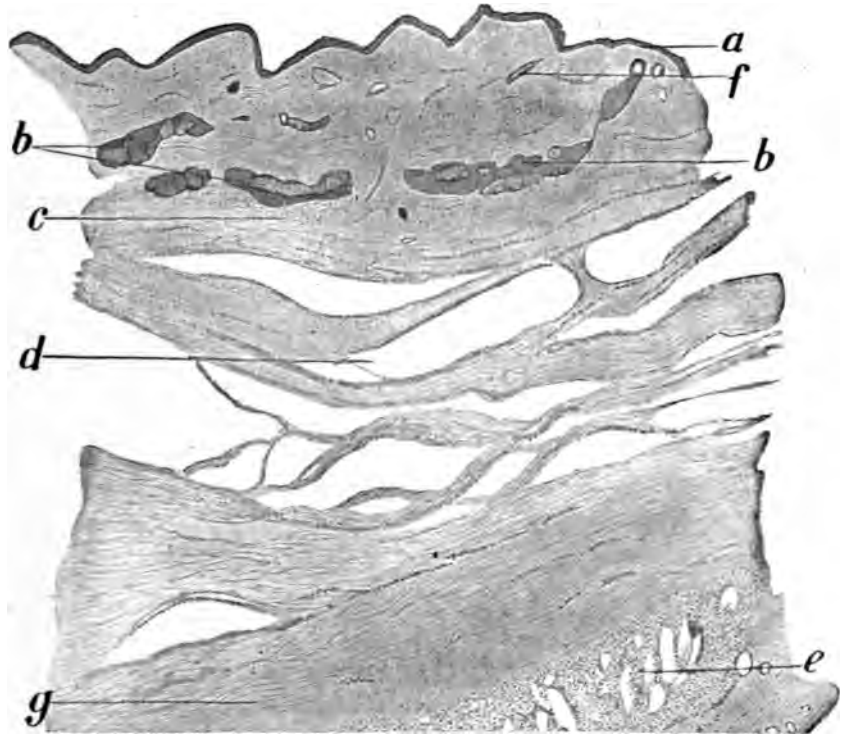


FIGURE 69.—SECTION THROUGH THE WALL OF AN OVARIAN DERMOID CYST.

a, stratified squamous epithelium lining the inner wall; *b*, sebaceous glands; *c*, fat tissue; *d*, connective tissue showing myxomatous degeneration; *e*, vessels in a layer of small-celled infiltration; *f*, section of a hair; *g*, fibrous connective tissue.

(β) Myoma.

Myomata of the ovary are very rare, and when they occur are always combined with fibromata.

(γ) Sarcoma.

Sarcomata are rare and are usually mixed tumors. Sarcomata derived from vessels are relatively most frequent (endothelioma, perithelioma). There also occurs, though rarely, a sarcomatous degeneration of the wall of papillary cystomata and dermoid cysts. Usually they are round-celled sarcomata and of a soft consistence.

3. The Dermoid Cysts.

Dermoid cysts differ from other ovarian cysts in that the inner lining of the wall has the character of the integument of the external surface of the body. We distinguish simple and complicated dermoids, the latter being also called "teratomata."

In the simple dermoids the lining of the inner wall of the cysts consists of squamous epithelium with papillæ which are very much like those of the external skin. In the underlying tissue are sebaceous glands and hair. The wall consists, in addition, of fibrous connective tissue in which myxomatous changes are frequently observed. In many places numerous vessels are found. In the walls of these cysts are found most remarkable structures, whose origin is entirely puzzling. I observed in one case, which is illustrated, a layer of the wall consisting mainly of giant cells. The contents of the simple dermoids consist of a greasy, yellow-colored substance, like the contents found in atheroma of the skin. As a general rule they do not reach a very large size. In the contents are found hair, loose or in bundles.

The simple teratomata contain, in addition, bone in pieces or as flat structures and also teeth. The complicated forms contain various structures of the body, and may consist of most varying tissues, such as brain substance, nerves, mammary tissue (?), etc. (See Part III.)

It should be remarked that the contents of dermoid cysts may be infectious. The rupture of these cysts during operation has frequently caused death from septic peritonitis.

PAROVARIUM.

1. NORMAL ANATOMY.

Between the ampulla of the tube and the ovary lies the parovarium, the remains of the sexual portion of the Wolffian body. It consists of a row of communicating canals which are lined with ciliated epithelium.

Parovarian Tumors.

The parovarium is of practical value because very large cysts originate from it. These have a very thin, translucent wall and generally clear watery contents. The inner lining is almost always ciliated epithelium, even in larger cysts. These cysts are macroscopically recognizable, for the ovary is distinctly separated from them while they lie in close contact with the tube. The parovarian cysts generally contain only one chamber.

The parovarium has received considerable attention through the

studies of v. Recklinghausen, who is of the opinion that the *adenomyomata* and *cystadenomata* of the uterus and tubes originate from epithelial remnants of the Wolffian body. The glands which are found in these myomata correspond in their arrangement and structure to the structure of the glandular elements of the Wolffian body, point for point. As regards the relative dependence of the glands and the muscle tissue in these adenomyomata, v. Recklinghausen has arrived at the conclusion,

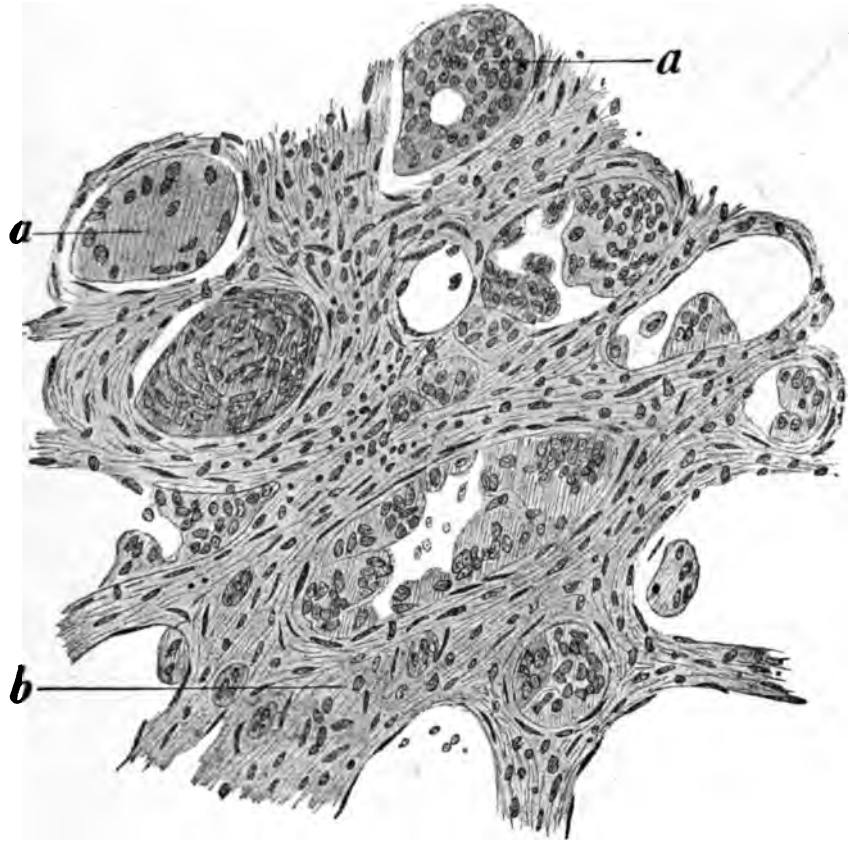


FIGURE 70.—FROM THE WALL OF A DERMOID CYST.
a, giant cells; *b*, connective-tissue stroma with spindle cells.

which I shall quote literally because of its importance: "In all smaller tumors of the body of the uterus and the tubal cornua the formation of muscle fibres goes hand in hand with the adenomatous formation and is proportional, which is the more evident the more distinctly muscle fibres are formed around the tubular glands and the groups of glands. Where this condition is most fully developed, and where the moiré strands appear most distinctly, there *the glands are to be considered as the real cause* of the myomatous formation. Just as during the embryonal

period the epithelium is first present, before the connective tissue and the enveloping muscular tissue, so also in its later growth does the gland become surrounded with a myomatous sheath only after it is itself completed. This sheath is therefore formed secondarily, and later on it may react upon the glandular structures and cause processes of growth in them." It is not sufficient to accept these remnants of the Wolffian body alone as the cause of the larger tumors of this form. In such cases all

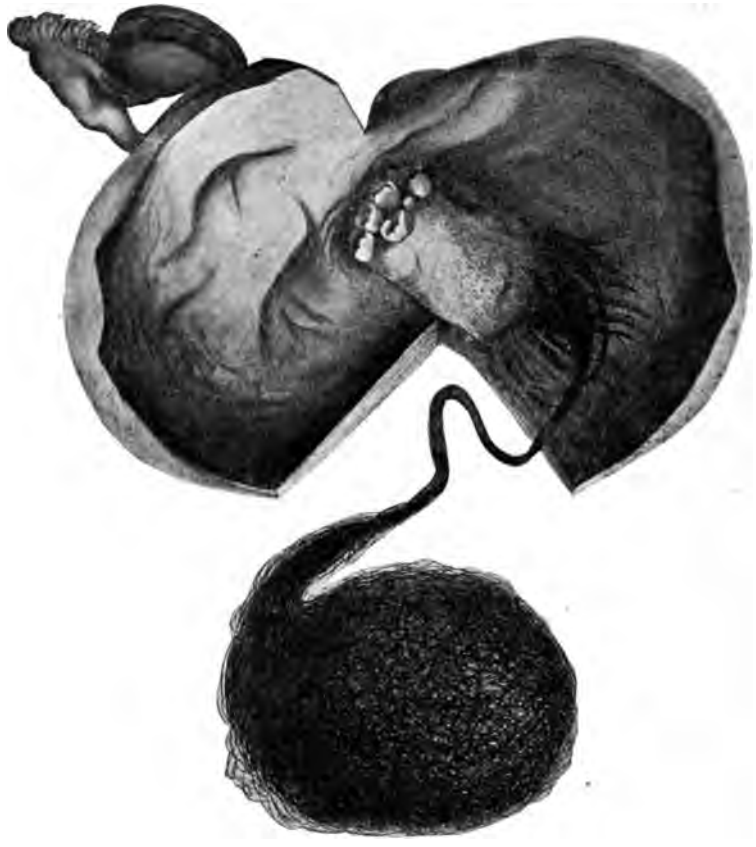


FIGURE 71.—TERATOMA OF THE OVARY.

The cyst is opened. Within is seen the skin-like inner wall with pores and a bone resembling a jaw in which are firmly embedded seven teeth. From the other end of the skin covering this bone grows hair which has formed a long, dense lump.

those conditions must have been present which make muscular tissue sensitive and likely to hypertrophy. Even though these valuable investigations have given those myomata a distinct position because of their origin, they are still to be distinguished by their location and their rougher structure from the ordinary myomata. v. Recklinghausen says:

"The adenomyomata occur most frequently in the body of the uterus on the dorsal wall, and in the tubal cornua on the cranial side. They

grow either from isolated cell centres and form large masses, generally in the vascular and in the *peripheral layers* of the wall, or else they occur in numerous centres close to each other, or else quite scattered without any demarkation from the remaining substance and are not limited to any layer of the uterine wall. They may make their way into the inner layers of the uterus and tube wall, and form *central* tumors."

The majority of examiners who have tested these observations on their own material have come to the same conclusion as v. Recklinghausen. That these examinations have not a theoretical anatomical interest alone is proven by the clinical observation that these tumors occupy a special position and demand a different therapeutic treatment from the ordinary myomata. *The prognosis of this affection is,* according to Freund, who states his views in connection with v. Recklinghausen's work, *much graver than is the case with the ordinary myomata.* On account of the presence of the numerous epithelial formations there is also greater danger of carcinomatous degeneration. (See Part III.)

PART III.

EMBRYOLOGY OF THE FEMALE GENITALIA AND THE PATHOLOGICAL GROWTHS DEVELOPING FROM EMBRYONAL STRUCTURES.

No region of the body goes through more interesting and important changes in the process of embryonal development than does the urogenital system. We find at first the formation of the "head kidney," or *pronephros,* with its excretory duct, the Wolffian duct. Its place is then taken by the *mesonephros,* or Wolffian body, with the same excretory duct. Both are replaced by the permanent kidney, or *nephros,* the Wolffian body becoming the parovarium and the duct becoming the canal of Gartner. We observe their close relation to the ducts of Müller (tube, uterus, vagina), and finally to the formation of the sexual gland (ovary).

Already in connection with the formation of the primitive furrow a development of part of the pelvic organs is observed, namely, the cloaca with its subsequent divisions, the urogenital sinus and the end intestine, and their openings, the urogenital opening (vestibulum) and the anal opening. From the very beginning there is an intimate connection between the end intestine and the genital and urinary passages.

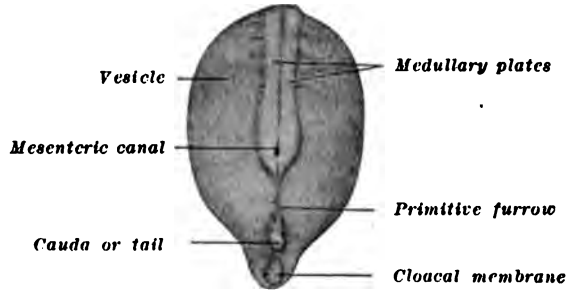


FIGURE 72.—SCHEME OF EMBRYONAL VESICLE, CAUDAL END. *(Waldeyer.)*

This may be seen in Fig. 72, which shows schematically the posterior end of an embryo on its vesicle. The medullary plates (tori medullares) are not yet closed, so that the external opening of the neurenteric canal is visible. The following portion of the primitive furrow (sulcus primitivus) is closed. Posteriorly is the cloacal membrane where the anus perforates later. Anterior to this the cells of the primitive trace, through

decided growth, have formed the caudal tubercle or "tail." At the cloacal membrane the intestine ends blindly. On the anterior surface appears the beginning formation of the allantois.

Fig. 73 shows in transverse section the middle blastodermic layer of a human embryo, still without primary vertebræ and chorda. Through subsequent division of the mesoderm it is separated and *segmented* into two layers, a parietal and visceral. There results then a symmetrical space

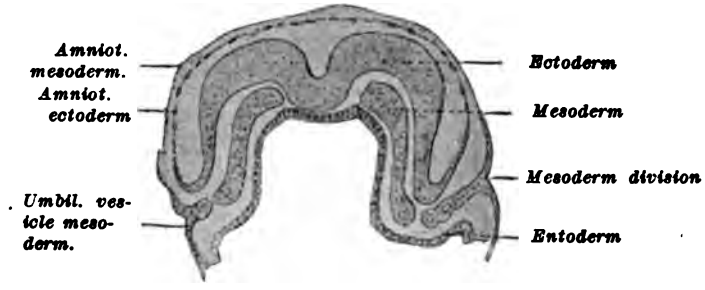


FIGURE 73.—MIDDLE BLASTODERMIC LAYER OF A HUMAN EMBRYO, STILL WITHOUT PRIMARY VERTEBRAE. TRANSVERSE SECTION. *(Keibel.)*

called "*celom,*" the walls of which gradually approach in the anterior median line and form the cylindrical body shape through their union, with resulting closure of the intestinal canal and the body wall (Fig. 74).

This space in the embryonal body, called "*celom,*" is intended to accommodate the internal organs or viscera. It is divided into three spaces: 1, primitive pericardial space; 2, the pleural spaces; 3, the abdominal cavity (Fig. 75).

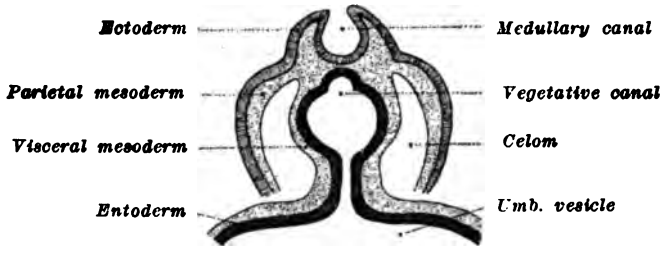


FIGURE 74.—ANIMAL AND VEGETATIVE CANALS. SCHEMATIC. *(Kollmann.)*

The *parietal* layer of mesoderm (the celom wall [Fig. 75]) consists of mesoderm from which develop the connective tissues and involuntary pale muscle fibres. Externally it is covered by ectoderm and internally by the celom epithelium, which consists of mesoderm cells.

The *visceral* layer of the mesoderm also covers, on the posterior body wall, the entire intestinal canal (Figs. 74 and 75), forms the intestinal mesenterium commune (Fig. 80), and furnishes the muscle layers for the intestine, and connective tissue cells and muscle fibres for its mucosa. It

is, therefore, naturally lined by entoderm, and is itself covered externally by celom epithelium. This epithelium is, as may be seen later, the point of location for the formation of the generative organs.

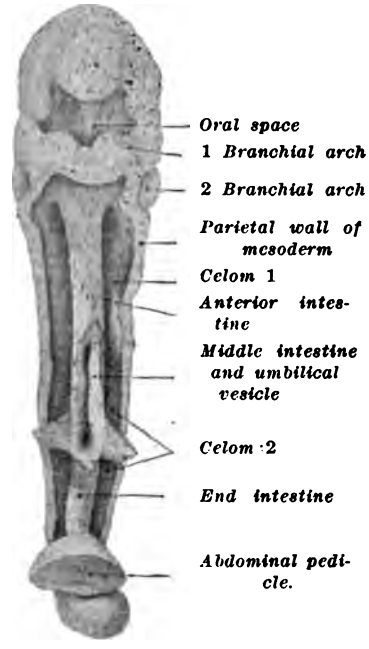


FIGURE 75.—HUMAN EMBRYO, 2.4 MILLIMETRES LONG, WITH HEART AND UMBILICAL VESICLE REMOVED AND UMBILICAL PEDICLE CUT. *(After His.)*

The lower end of the intestine *(D)* may be seen in Fig. 76. It empties into a blind sac *(cloaca)*, which is continued into the tail-like end of the

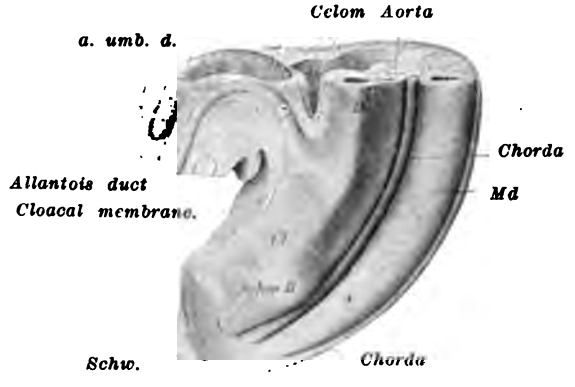


FIGURE 76.—CAUDAL END OF EMBRYO 3 MM. LONG. RECONSTRUCTION. *(Keibel.)* *Cl.*, cloaca; *Md.*, medullary canal; *Schw.*, tail; *Schw. D.*, caudal intestine.

body *(Schw.)*. The cloaca is an entodermal space into which the allantois duct empties ventrally and the intestine dorsally. The allantois duct also comes from this general entodermal space. That part of the

allantois caudal to the duct, and which is a continuation at the expense of the cloaca, does not really constitute the allantoic duct. A sharp line between the original ventral portion of the cloaca and the allantois does not exist. In embryos of three millimetres the medullary plates are not yet closed. The caudal intestine *(Schw. D.)* is present in the tail. This

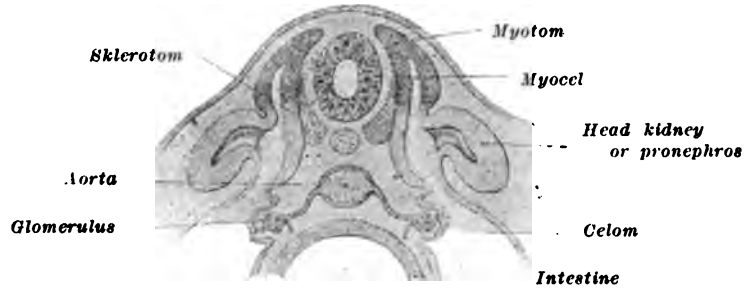


FIGURE 77.—TRANSVERSE SECTION IN THE REGION OF THE PRONEPHROS, OR HEAD KIDNEY (ICHTHYOPHIS GUT). *(After Semon.)*

caudal intestine is situated behind the location of the future anus, and is therefore called "post-anal intestine." In Fig. 76, an embryo of fifteen to eighteen days, the cloacal membrane does not cover the entire cloaca.

PRONEPHROS.—In the parietal mesoderm, where the segmented portion goes over into the unsegmented, is situated the "middle plate." In this area the "head kidney," or pronephros, develops, consisting of a

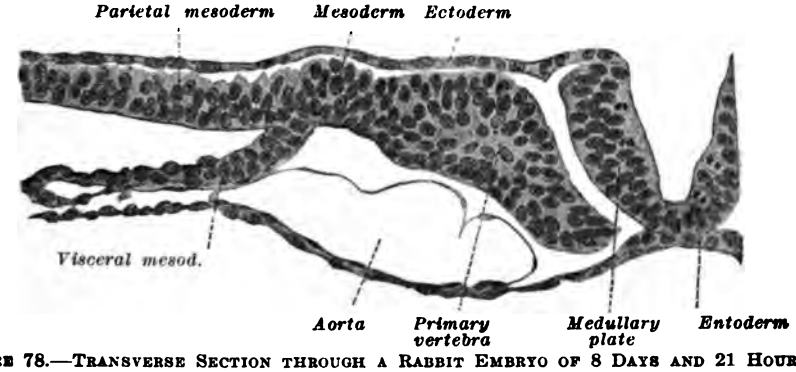


FIGURE 78.—TRANSVERSE SECTION THROUGH A RABBIT EMBRYO OF 8 DAYS AND 21 HOURS, WITH 10 PRIMARY VERTEBRAE, CAUDAL TO THE LAST PRIMARY VERTEBRA. *(O. Schultze and R. Bonnet.)*

series of tubules connected with the celom. Each opening into the celom is funnel-shape and ciliated. Each of these tubules is called "a diverticulum." At their peripheral ends these diverticula unite into a common canal which lies close to the ectoderm, the Wolffian duct. The duct extends over a considerable space, and is thus connected with the celom by several consecutive "head-kidney" tubules. These tubules lie near the aorta; their glomeruli develop to the right and left of the mesentery (Fig. 77).

MESONEPHROS.—The pronephros is retained in certain fishes. In

amphibiæ it disappears; in amniotæ evidences have been found. Remains have been described in rabbits, and evidences of its existence are claimed to persist in man, and it is probable that it develops in the same manner as in mammals.

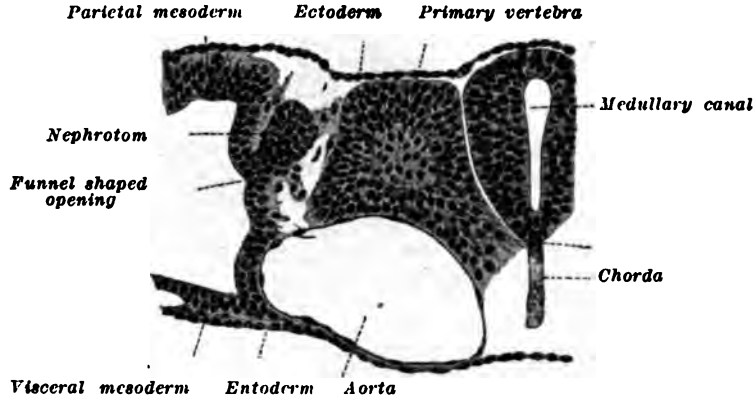


FIGURE 79.—TRANSVERSE SECTION THROUGH RABBIT EMBRYO OF 8 DAYS AND 23 HOURS, WITH 13 PRIMARY VERTEBRAE. *(O. Schultze.)*

Shortly after the formation of the pronephros, in animals in which its existence is only rudimentary, there develops the mesonephros, or Wolffian body. It originates immediately posterior to the pronephros on the following section of the Wolffian duct. Medial to the pronephros, between the middle plate and the primary vertebræ, the "blastoma" of the Wolffian body appears.

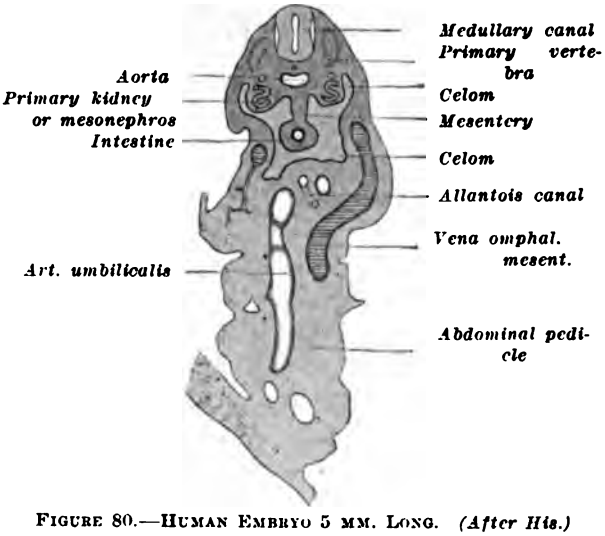


FIGURE 80.—HUMAN EMBRYO 5 MM. LONG. *(After His.)*
The transverse section includes the umbilical pedicle also.

From this develop, parallel to the formation of the segmental primary vertebræ, segmental bodies, or "nephrotoms," communicating with the celom by funnel-shaped spaces (Fig. 79).

These form the tubules of the Wolffian body, which at their outer end empty into the Wolffian duct. The Wolffian body thus develops at the side of the vertebræ and retroperitoneally. Its surface looks toward the celom. Medially it borders on the aorta, and posteriorly on the posterior body wall (Fig. 80).

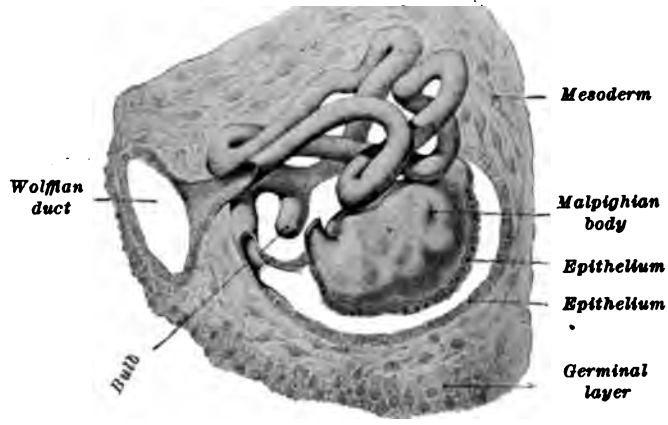


FIGURE 81.—WOLFFIAN BODY TUBULES, COMBINED DRAWING. HUMAN EMBRYO 10.2 MM. LONG. *(After Kollmann.)*

Near the celom develop capsules with glomeruli. The Malpighian bodies are like those of the kidney with Bowman's capsule and vessel knots. The tubules are twisted and lined with cuboidal epithelium; the part near the glomerulus is wide and is lined with large cuboidal CILIATED

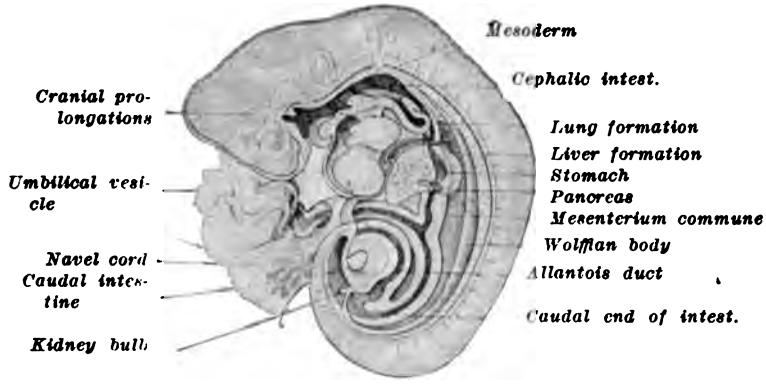


FIGURE 82.—HUMAN EMBRYO 5 MM. LONG. RECONSTRUCTION. *(After His.)*

cells having *secretory function.* Toward the duct the tubules become narrower, and, like the Wolffian duct, are lined with much lower cuboidal cells.

The proximal portion of the Wolffian body is of simple form and is called the "cephalic part." Its tubules at an early period lose their cap-

sules and glomeruli, and come into close relation with the sexual gland (ovary), and it is therefore called the "sexual part" of the Wolffian body. The distal part or caudal portion has secondary tubules united to the main or primary tubules. The Wolffian body extends down into the pelvis, its upper end extends up to and behind the heart (Figs. 82 and 95).

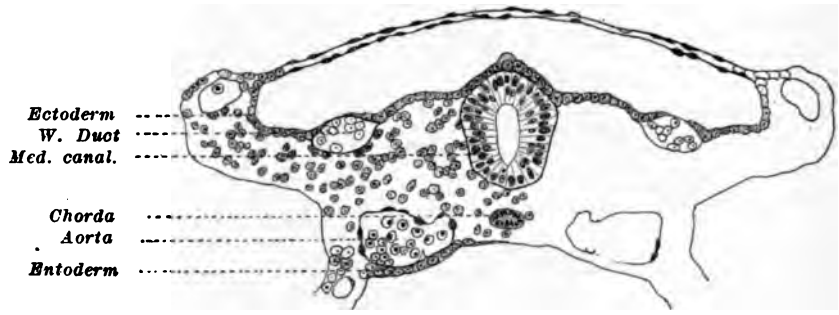


FIGURE 83.—TRANSVERSE SECTION THROUGH RABBIT EMBRYO, SHOWING ORIGIN OF WOLFFIAN DUCT FROM ECTODERM.

WOLFFIAN DUCT.—The excretory duct or Wolffian duct develops near the ectoderm. According to some it develops only near, according to others partly from, and according to most recent views entirely from, the ectoderm. It may be seen in Fig. 83 that the Wolffian duct has not yet entirely separated from the ectoderm. The Wolffian duct grows

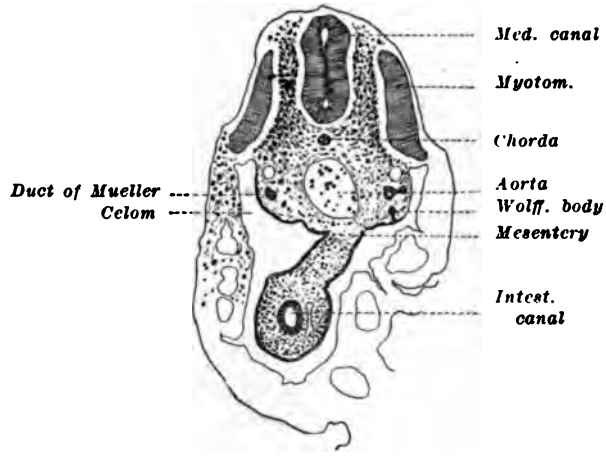


FIGURE 84.—TRANSVERSE SECTION THROUGH GUINEA-PIG EMBRYO.

downward by increase of its own cells, becoming further and further separated from the ectoderm until it reaches the cloaca.

After the formation of the cylindrical body shape the Wolffian duct is situated in its entire course near the celom close to the Wolffian body, as may be seen in Fig. 84.

The tubules of the Wolffian body have developed in the mesoderm from the so-called "nephrotoms." These are said to be part of the primary segments, the remaining portion of these segments forming the myotom (muscle plate) and the sclerotom, from which develops the skeletal tissue. Although these nephrotoms develop in mesoderm, Spee and others hold that their cells come partly or wholly from the ectoderm.

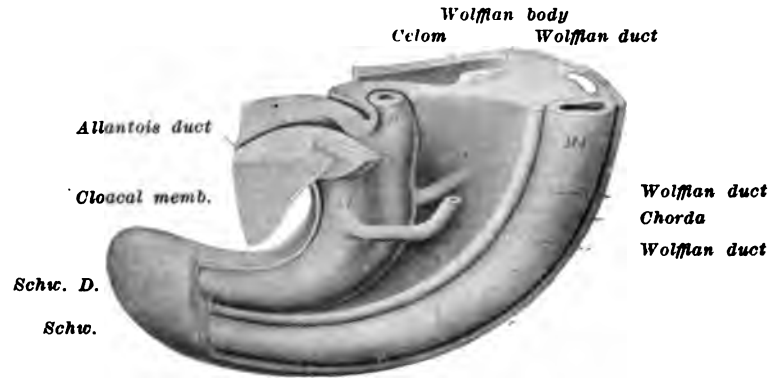


FIGURE 85.—HUMAN EMBRYO 4.22 MM. LONG. *(After Keibel.)* CAUDAL END.

In Fig. 85 are seen in section the celom, the Wolffian body and the Wolffian duct, and the entrance of the Wolffian ducts into the ventral portion of the cloaca. In embryos of three or four millimetres the Wolff-

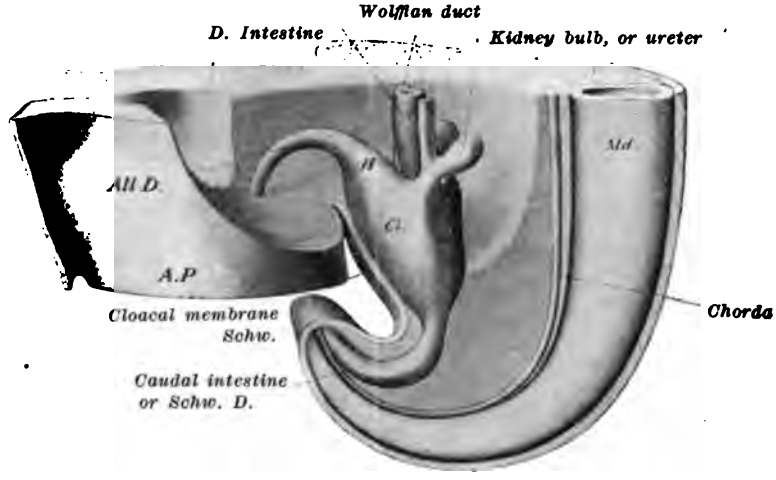


FIGURE 86.—CAUDAL END OF HUMAN EMBRYO 6.5 MM. LONG. *(After Keibel.)*

ian duct and the intestine empty at the same level into the entodermal cloaca. The extent of the cloaca is now greater, and is entirely covered by the cloacal membrane. The dilated portion above the letters *Cl*, Fig. 85, can no longer be considered a part of the allantoic duct, for this dilatation is to form a portion of the future bladder. In Fig. 85 the

medullary canal, chorda, and caudal intestine are closely united in the tail. Further up the chorda is separated from the end intestine.

In Fig. 86 the cloaca is smaller, and the caudal intestine is clearly marked off from the cloaca. The cloaca is now continued dorsally into the true intestine, and ventrally into the primary formation of the bladder *(H)*. The Wolffian duct *(Wf.D.)* empties into the cloaca in the area which marks off the cloaca on the one hand from the intestine *(D.)* and the bladder on the other. The part of the cloaca into which each Wolffian duct enters belongs to the future bladder and urethra.

URETER.—From the lower end of each Wolffian duct develops a kidney bulb, the primary formation of the ureter. It lies dorsal, but later lateral to the Wolffian duct (Fig. 86).

The prominent tail subsequently disappears at an early period. Between the tail and the primitive anus appears an epithelial lamella con-

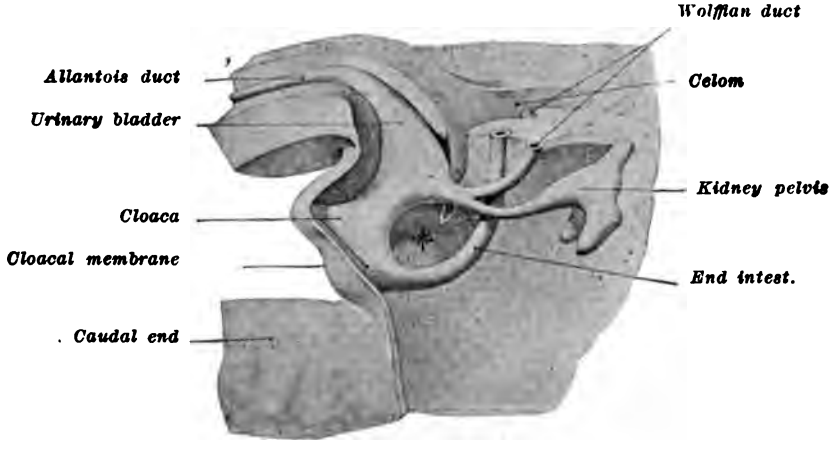


FIGURE 87.—PELVIC END OF HUMAN EMBRYO 11.5 MM. LONG (4½ WEEKS). *(After Keibel.)* *SEPTUM URO-RECTALE.

sisting of two layers, which, however, is only temporary. There occurs a growth of connective tissue between the primitive anus and the base of the tail, forming a prominence of mesoderm called "the post-anal prominence." Through the growth of the post-anal prominence the tail is deprived of its epithelial covering and the above-mentioned lamella is opened, the upper layer covering the lower surface of the post-anal prominence and the lower layer covering the ventral surface of the tail. The caudal intestine becomes gradually reduced to an epithelial strand. The tail also disappears under normal conditions. In the disappearance of this area the same processes take place as occur in the penis in large inguinal herniæ, where the penis is robbed more and more of its skin, through decided stretching of the surrounding tissues, until it disappears finally under the surface. By the withdrawal of this tail into the trunk epithelial remnants of the caudal intestine may also be carried along. Such epithelial remains would subsequently lie dorsal to the future

rectum—a point of importance with regard to rectal carcinomata and tumors of this region. At times the tail or the caudal intestine persists in human beings.

At a later stage intestine and bladder empty into a smaller cloaca and part of the future urethra is present (Fig. 87). The ureter now empties into the lateral wall of the Wolffian duct instead of the dorsal. The celom keeps pace with the gradual separation of the intestine on the one hand, from the bladder and urogenital sinus on the other hand. The cloaca has become partially divided into an anterior portion, the future bladder and urethra, and a posterior portion, the future rectum. Into the anterior division empty the Wolffian ducts and the ureters. The cloaca has been thus divided by two endothelial folds which unite in the middle line, forming a septum. This septum extends down toward the cloacal membrane and forms the primitive perineum. Mesoderm completes the division, forming the future urorectal septum. Mesoderm pushes the intestinal canal against the sacral vertebræ, and the anterior canal is pushed against the abdominal wall. We have then later, on extension

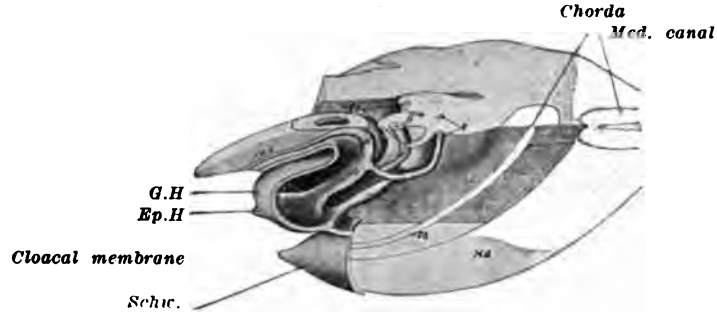


FIGURE 88.—HUMAN EMBRYO 14 MM. LONG. *(Keibel.)*

of the dividing membrane, the urogenital sinus, which is that part of the former cloaca below the entrance of the Wolffian ducts (Fig. 88).

In Fig. 88 the tail is small, but lies close to the still closed anal formation. The medullary canal still extends into the tail. A definite division between the urogenital sinus and the bladder is not distinct. The Wolffian ducts and the ureters now empty separately into the bladder. The celom has descended much lower, especially laterally. An opening for the urogenital sinus is present, and the genital prominence *(G.H.)* is well developed. The upper end of the cloacal membrane is represented by the epithelial prominence *(Ep.H.)*.

In embryos of twelve millimetres the allantoic duct is closed before reaching the umbilicus, and is only an epithelial strand. As at this period the glomeruli of the Wolffian body are secreting actively, Nagel claims that the cloacal membrane is already perforated. The view expressed above, that of Keibel, is undoubtedly correct, and the secretion of the Wolffian body gains an exit only in embryos fourteen millimetres long.

DUCTS OF MUELLER.—The ducts of Müller develop on the celom epithelium at the outer side of the Wolffian body. Each commences, in embryos of twelve millimetres, as a short funnel, open above, with a solid pointed end, and in its growth follows closely the course of the Wolffian duct until it reaches the cloaca. It is said by some, for this reason, that the ducts of Müller are in part or whole given off by the Wolffian duct, but this is not probable (Fig. 89).

At times the inversion of the celom epithelium is repeated, so that a longer or shorter accessory tube is formed. An entirely double duct of Müller has been found on one side, and accessory tubal ostia not so rarely. The accessory tubes are usually shown by a more or less distinct fimbriated end in the region of the abdominal opening of the normal tube. These are to be distinguished from accessory openings in the tube itself, which may be formed through a union between the epithelium of the

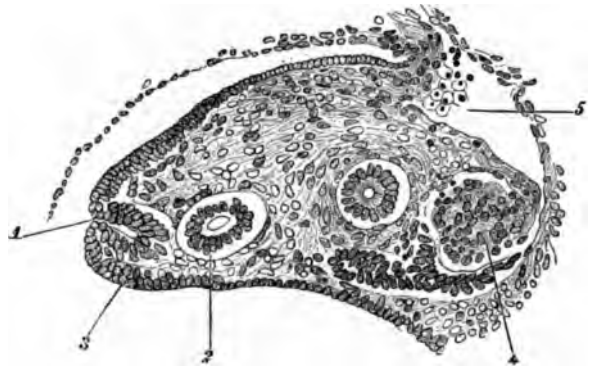


FIGURE 89.—TRANSVERSE SECTION THROUGH THE UPPER END OF THE WOLFFIAN BODY OF A FEMALE EMBRYO 12 MM. LONG. *(Nagel.)*

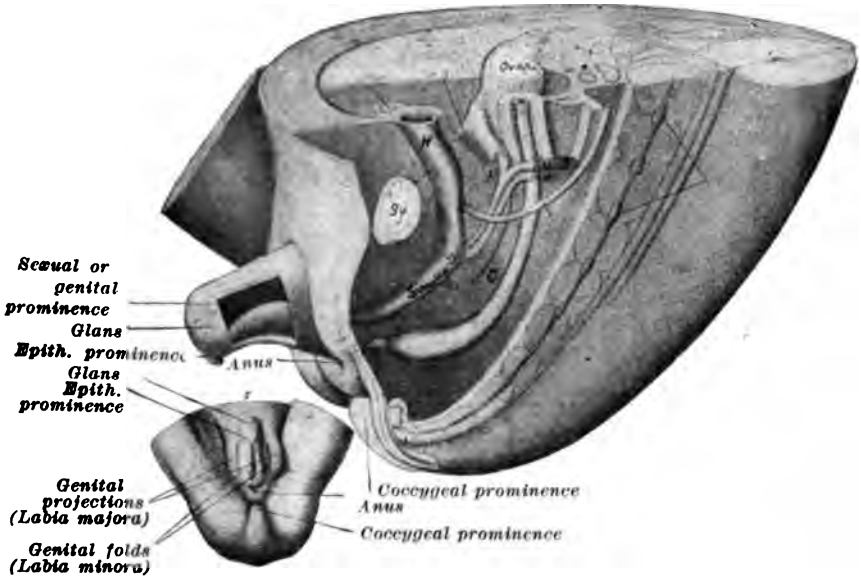
1, duct of Mueller; 2, Wolffian duct; 3, celom epithelium of the mesonephros; 4, a glomerulus of the Wolffian body; 5, blood vessel.

duct of Müller and that of the Wolffian duct—a fact which perhaps explains the view that the former is a product of the latter. Such accessory openings may result from thinning and perforation of the tube wall at such points of union. There are found in the walls of these tubes thinned spots, through which the mucous membrane may be recognized. These may, however, result from imperfect closure of the original funnel-shaped inversion. The ducts of Müller enter the urogenital sinus in embryos of twenty-five to thirty millimetres. The end of each duct is solid. The ends of the duct of Müller cause a prominence in the urogenital sinus, called "the prominence of Müller" (Fig. 94). The ureters are now situated cranially to the Wolffian ducts.

The area above the point *S*, Fig. 90, is the future bladder and urethra. The opening of the Wolffian ducts marks the division between the future urethra and the urogenital sinus. The wall between the two ducts becomes the hymen.

CLOACAL MEMBRANE.—The cloacal membrane is in greatest part entodermal, and only partly ectodermal. It appears to develop from the posterior end of the primitive trace. In embryos of 4.2 mm. it extends over the entire end of the cloaca (Fig. 85). The frontal dividing wall mentioned above has divided the cloacal membrane into an anterior part or *urogenital plate,* and into the *anal membrane* which closes the intestine and which later marks the division between the ectodermal and entodermal portions of the rectum. The perforation for the urogenital sinus occurs earlier than that for the anus.

The area where the anus perforates is represented by a groove, the *anal groove.* From here the now elevated cloacal membrane extends between the sexual folds of the genital prominence, forming the cloacal



H, bladder; *S*, point of future hymen; *C*, fold of Douglas.
FIGURE 90.—CAUDAL END OF HUMAN EMBRYO 29 MM. LONG. *(Keibel.)*

plate. Its upper end forms the epithelial prominence. The cloacal plate is not perforated so long as any cloaca remains. When the cloacal plate becomes thinner and thinner it still covers the entodermal sinus and the entodermal intestine, the sexual prominence, the anal groove, and divides the primary perineum into a right and left perineal half, which pass anteriorly into the sexual folds. These halves (mesodermal) pass posteriorly into the anal region as anal prominences. The space (imaginary) covered by the cloacal plate has been called "ectodermal cloaca." As said before, the opening for the sinus occurs first, and later, in the ninth week, that for the anus. The perineum is formed by the union of the perineal folds in the middle line forming the perineal raphé. The sexual folds form the labia minora, the sexual or genital prominence

forms the clitoris. The anus develops entirely IN THE REGION OF THE ECTODERM. The anal prominences, mesodermal, unite above the primitive perineum and surround in this manner the above-mentioned *ectodermal anal groove.*

After the formation of the permanent perineum, the ectodermal

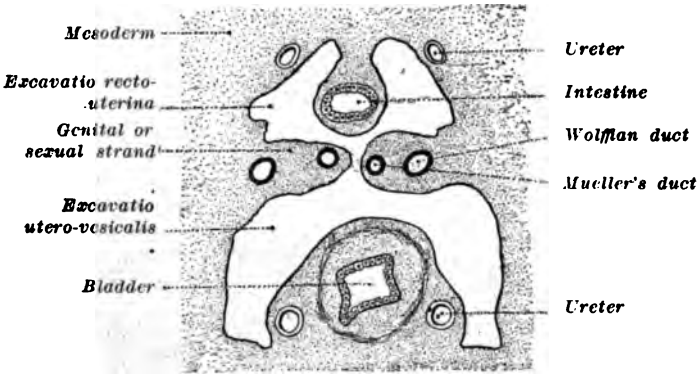


FIGURE 91.—PELVIC END AT THE LEVEL OF THE BLADDER, WITH THE GENITAL OR SEXUAL STRAND OF THE LEFT AND RIGHT SIDES. HUMAN EMBRYO OF 9 WEEKS. *(Kollmann.)*

cloaca has been divided into the ectodermal sinus urogenitalis and into the ectodermal intestine (anus). The former becomes that part of the vestibule of the vagina which is surrounded by the previously mentioned sexual folds (labia minora). These changes may be observed by a comparison of Figs. 88 and 90.

Into the celom there project from the dorsal wall of the body three

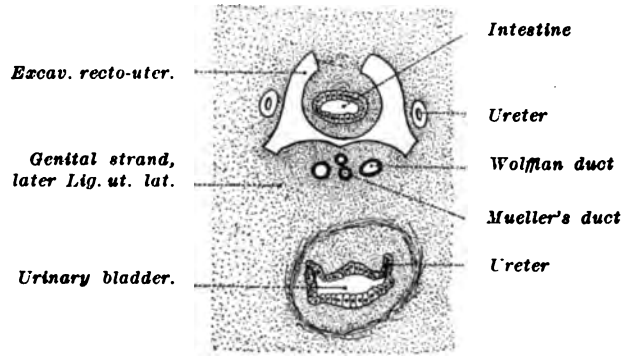


FIGURE 92.—GENITAL OR SEXUAL STRAND. HUMAN EMBRYO OF 9 WEEKS. TRANSVERSE SECTION. *(Kollmann.)*

folds, one containing the intestine and the other two containing the ovary, Wolffian body, Wolffian duct, and the duct of Müller of either side (Fig. 91).

From the ventral wall is a fold in which is situated the bladder. In Fig. 91 the folds containing the ducts of Wolff and of Müller have not yet

united. A section made a little further down shows these folds, called "genital strands," united, and the celom has thus been divided into an anterior and a posterior division.

The stroma of the Wolffian body is a richly vascular embryonal connective tissue or myxoid tissue. The Wolffian body is enclosed in a mesentery which becomes more distinct and movable when the Wolffian body begins to disappear. The distal continuation of the Wolffian body is the *urogenital fold.* Since this fold makes a spiral twist, so each duct of Müller lying in it, while situated in its upper part external to the Wolff-

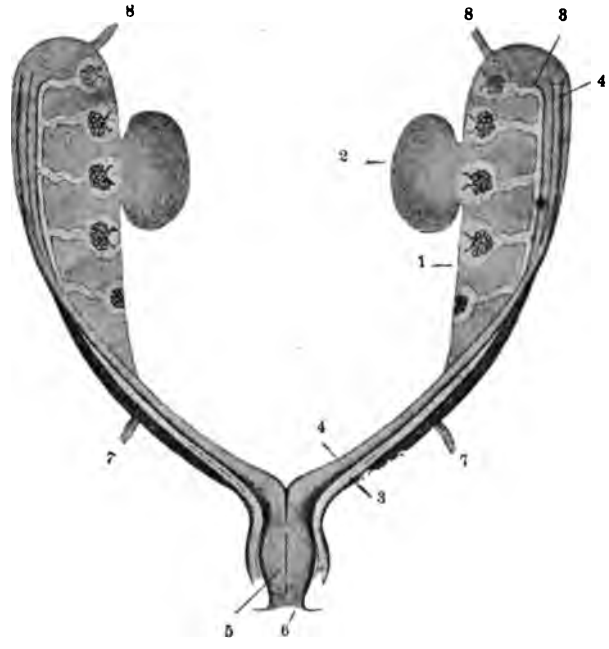


FIGURE 93.—SCHEMATIC FIGURE OF THE INTERNAL GENITALIA OF A FEMALE HUMAN EMBRYO OF ¼ CENTIMETRE. *(Nagel.)*

1, Wolffian body; 2, sexual gland (ovary); 3, Wolffian duct; 4, duct of Mueller; 5, genital strand; 6, opening of lower end (future vagina) of genital strand into the urogenital sinus; 7, gubernaculum Hunteri; 8, diaphragmatic band of the mesonephros.

ian duct, makes a spiral twist in its lower part and lies *internal* to the Wolffian duct (Fig. 93). The ducts of Müller enter the urogenital sinus in embryos of twenty-six to thirty millimetres. The end of the duct is solid. Since the ureter is situated higher up at this time, we have two Wolffian ducts and two ducts of Müller entering the urogenital sinus, forming the "prominence of Müller." The intervening tissue forms the future hymen (Figs. 93 and 94).

The folds in which the ducts of Müller are situated have united, and so have the ducts of Müller. As mentioned, the tissue in which the ducts of Müller and the ducts of Wolff are surrounded is called "the genital strand."

Fig. 94 shows the prominence of Müller *(Mü.P.)*, the ducts of Wolff

(Wf.D.), the ducts of Müller *(Mll.D.)*, the ureter *(U.)*. *Tr.L.* represents the trigonum vesicæ. We see the ducts of Müller united down to their lower end, where they again separate, bending forward at a sharp angle. The ducts of Wolff begin to retrograde, and in embryos of four centimetres only the ducts of Müller enter into the urogenital sinus. The upper end of the mesentery of the Wolffian body extends to the diaphragm and becomes the diaphragmatic band, or *plica phrenico-meso-nephrica* (8, Fig. 93). From its lower end extends the *plica inguino-meso-nephrica*. In it are strands of muscle fibres with connective tissue. It is attached proximally to the ducts of Wolff and Müller at the point where the ovarian ligament is also situated. It extends distally into the subperitoneal tissue of the abdominal wall and into the region of the future inguinal ring (7, Fig. 93). On the disappearance of the Wolffian duct it enters into the uterine wall. From the lower end of the sexual gland extends the fold of the Wolffian body. In it is a band of muscle fibres and connective tissue attached to the closely grouped Wolffian and

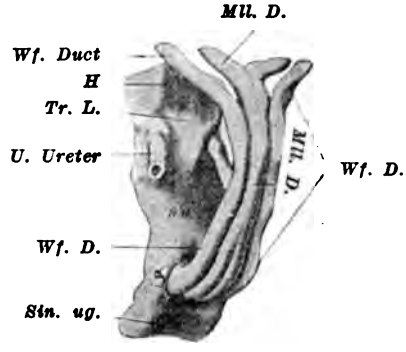


FIG. 94.

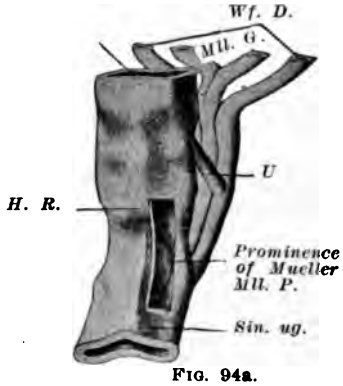


FIG. 94a.

FIGURE 94.—DUCTS OF MUELLER AND WOLFF, ETC., OF FIGURE 90 MAGNIFIED.

Müller ducts. It represents the ovarian ligament. As the Wolffian duct disappears it is connected later only with the duct of Müller.

The ducts of Müller form an angle which marks off the lower end of the tube from the beginning of the uterus. It is from this point that the gubernaculum Hunteri, the future ligamentum teres, is given off. The first union of the ducts of Müller occurs in the eighth week. The union is complete at the third month up to the ligamentum teres. Even at this time the utero-vaginal canal shows a curve with its concavity anteriorly. The walls of the tube and uterus come from the mesodermal elements of the Wolffian body (and the urogenital fold).

VAGINA.—The vagina develops from the lower end of the ducts of Müller. The final separation between the vagina and uterus is found in embryos of ten to fourteen centimetres, although at an earlier period the distinction is evident through a difference in the character of the epithelial cells. The vagina develops from the lower end of the ducts of Müller. At the same time the urogenital sinus becomes shorter. With the growth

of the vagina and the shortening of the sinus the formation of the urethra goes on. The longer the vagina and the shorter the sinus the nearer does the opening of the urethra approach the cloacal groove, until it and the vagina assume their normal situation, the sinus forming the vestibule. The portion of the vestibule of the vagina immediately surrounding the urethral opening, and the external opening of the vagina, the upper surface of the hymen, and the region of the openings of the glands of Bartholini, belong to the *entodermal urogenital sinus*. The ectodermal urogenital sinus forms that part of the vestibule covered by the labia minora.

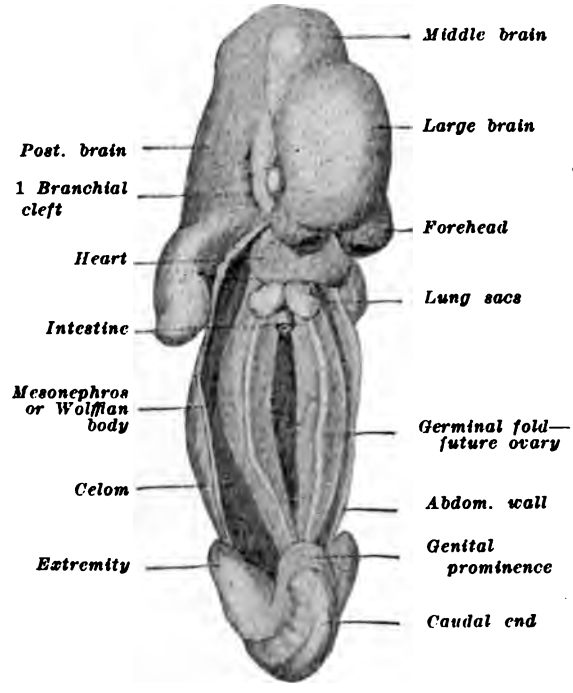


FIGURE 95.—HUMAN EMBRYO IN THE FIFTH WEEK, THE ANTERIOR BODY WALL REMOVED, THE MESONEPHROS EXPOSED. *(Kollmann.)*

As soon as the ureters enter independently into the cloaca (12-13 mm.) the development of the bladder begins through the change of this anterior portion of the cloaca into a spindle-shaped tube. The part not used for the bladder forms the urachus. Through growth of the future trigonum the entrance of the ureters is more and more separated from the Wolffian ducts. It must be mentioned that Minot and others consider the anterior part of the cloaca, which the Wolffian ducts and ureters enter, as belonging to the allantois and not to the cloaca. As cloaca and allantois are both derived from the same entodermal space such a distinction cannot be clearly defined.

KIDNEY.—The ureter lies at first dorso-medial, then dorsal, and

then dorso-lateral. Its upper end develops, forming the pelvis of the kidney. From it develop the kidney calyces, and from these the kidney tubules. According to certain authors, the canal system of the kidney comes from the ureter, according to the usual form of glandular growth. According to others the kidney develops from two separate formations: the medullary substance and the collecting tubules from the ureter, the cortical substance and the twisted tubules from a specific formation, the kidney blastoma.

OVARY.—In embryos of eight to twelve millimetres the celom epithelium on the inner side of the Wolffian body becomes thickened.

This constitutes the germinal fold, which has been outlined distinctly from the stroma of the Wolffian body. Through a decided increase in the cells of this germinal epithelium and a change of a large part of these cells into primitive ova, the parenchymatous ovary is formed. Connec-

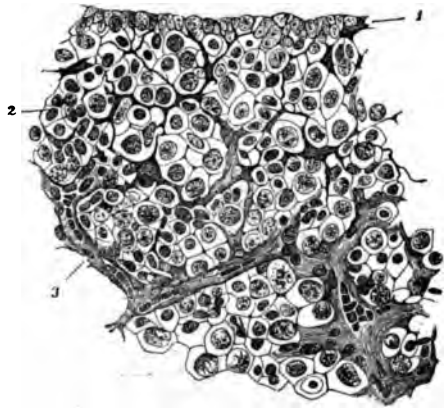


FIGURE 96.—SECTION THROUGH THE OVARY OF A HUMAN EMBRYO WITH A BODY LENGTH OF 11 CENTIMETRES. *(Nagel.)*

1, External layer of primary ovary (later germinal epithelium of the ovary); 2, compartments of ova; 3, stroma (vessels).

tive-tissue cells and vessels grow *from the stroma of the Wolffian body* into the germinal epithelium, dividing it into compartments. These compartments consist of primary ova and germinal epithelia, and are divided into constantly smaller compartments by the growth of connective-tissue stroma.

Finally, we have primary ova surrounded by a layer of germinal epithelium, the so-called "primary follicles." The superficial layer of the germinal epithelium remains as a simple layer of cylindrical epithelium covering the ovary. Most authorities believe that the follicle epithelium is derived from the germinal epithelium. Others claim that it originates from the connective-tissue stroma of the Wolffian body.

As regards the germinal epithelium, it is said to originate from the celom epithelium, which is itself mesoderm. It may be said that Spee and others hold that the germinal epithelium is a derivative of ectoderm

cells carried to their point of development by the Wolffian duct and the Wolffian body. That this is possible may be seen by a comparison of Fig. 83, where the Wolffian duct lies near the ectoderm, and Fig. 84, where all these structures are situated near the celom to the right and left of the intestinal mesentery.

In the descent of the ovary the gubernaculum Hunteri plays an important rôle, for the ovary may be carried into the canal of Nuck.

The follicles in the ovary, after their formation, are forced more and more into the periphery, and in the newly-born we can see the connection between the youngest primary follicles and the germinal epithelium covering the ovary. These are not to be confused with depressions and furrows found on the surface of the ovaries of the newly-born. The majority of ova and primary follicles degenerate during intrauterine life and in the first year. Their place is taken by loose connective tissue. Finally, we have a surface layer with primary follicles, called "zona

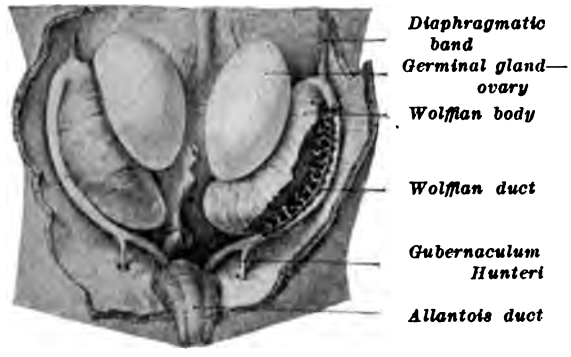


FIGURE 97.—WOLFFIAN BODY AND GENERATIVE GLAND (OVARY), HUMAN EMBRYO 17 MM. LONG, AT BEGINNING OF THE SIXTH WEEK. TO THE RIGHT THE WOLFFIAN DUCT IS OPENED. *(Kollmann.)*

parenchymatosa," and a deeper layer of connective tissue and vessels, called the "zona vasculosa."

In the development of the ovary there pass out from the germinal epithelium thinner or thicker cell bands, the so-called "tubules of Pflüger." In them are found follicle cells and ova. The epithelial prolongations which grow out of the Wolffian body into the ovary, and which penetrate the ovary, are so-called "sexual bands" of the primary kidney. They originate from the epithelium of the Malpighian bodies, and extend toward the tubes of Pflüger. From the latter develops the cortex of the ovary; the former take part in the formation of the medullary portion and are called "medullary bands."

According to Nagel, those connective-tissue cells which divide the germinal glands into compartments originate from the stroma of the Wolffian body, without participation of the Wolffian canals.

DUCT OF GARTNER.—The Wolffian ducts, if retained, would lie

in the fornix and the upper lateral wall of the vagina, and not in the anterior vaginal wall. The Wolffian duct becomes the duct of Gartner, and is sometimes present in the wall of the uterus and in the fornix. Nagel says it extends as far as the vaginal portion of the cervix. Beigel and Dohrn have found it along the vagina. Ackermann has followed it down to the hymen. Klein followed it, in the newly-born, from the parovarium into the uterus and to the wall of the cervix. On the other side it extended from the parovarium to the broad ligament, into the body of the uterus and into the cervix wall, where it took an S-shaped curve through the fornix and along the vagina. Branches of the duct of Gartner are often given off into the uterine substance.

Parovarium.

Epoöphoron.—On the development of the kidney the Wolffian body retrogrades. The upper or "sexual part" (epoöphoron) is usually re-

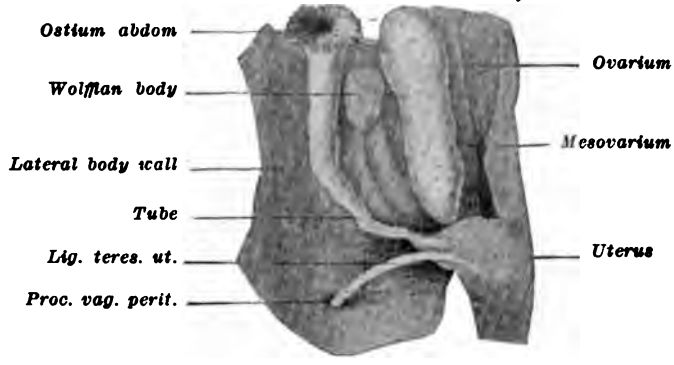


Figure 98.—Tube, Uterus, and Ovary of the Right Side at the Beginning of the Third Month. *(Kollmann.)*

tained, and in the late fetal period suffers little change of location. In the newly-born it is often atrophied. It lies in the mesovarium and mesosalpinx, between the ovary and the tube, with variations in the size and number of its tubules. The tubules run into the duct of Gartner, which lies parallel to the Fallopian tube and at right angles to the tubules. In the epoöphoron are found pseudoglomeruli, which are not regressive ones, but immature later formations in the fetal period. This is evidenced by the fact that the epithelium of these glomeruli is well preserved. In the tubules is found *ciliated epithelium,* and their walls contain *smooth muscle fibres.* The tubules usually end blindly at the hilus, but may *extend into the ovary even up to its surface.* It is to be mentioned that during its development the epoöphoron is not situated very near the duct of Müller.

Paroöphoron.—The paroöphoron, or yellow body of Waldeyer, is what remains of the lower distal portion of the Wolffian body. Malpighian

bodies are still found in the fourth intrauterine month, but rarely in adults. According to Waldeyer, the paroöphoron is found in adults in the broad ligament medial to the epoöphoron and often extending up to the uterus. It is composed of small, round or long bodies which are blind tubules filled with epithelial cells, cell detritus, and pigment, giving this structure a brownish or yellowish color. The tubules anastomose frequently. The paroöphoron is more rarely found than is the epoöphoron.

Aschoff believes the paroöphoron of Waldeyer to be the continuation of the proximal or "sexual portion" of the Wolffian body, instead of representing the distal or secreting portion. He finds the latter, after descent of the ovary, below and lateral to the epoöphoron. Meyer finds the paroöphoron in the fetus of two or three months to be on the posterior abdominal wall, to the right and left of the vertebræ, and lateral and an-

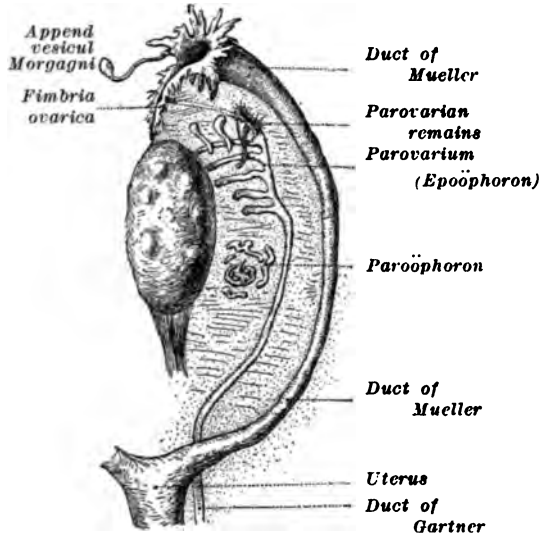


FIGURE 99.—RELATION OF THE WOLFFIAN DUCT AND THE DUCT OF MUELLER IN THE FEMALE EMBRYO. *(Schematic after Kollmann.)*

terior to the uterus. It is situated in a peritoneal fold which goes over into the broad ligament. On descent of the adnexa the paroöphoron is carried further and further from the posterior abdominal wall, downward and laterally into the broad ligament, according to the insertion of the latter. Since the base of the broad ligament in its development comes to lie more and more laterally, the paroöphoron is also carried along, with the exception of such remnants *as may be left more medially or on the posterior abdominal wall.* Its situation in the mesial portion of the broad ligament near the uterine border is not the usual one, according to Meyer.

Cilia are characteristic of certain areas of the parovarium. 1. Even in the early embryonal period the epithelium of certain areas of the Wolffian body tubules, and in fact those cells which are high cylindrical

at their height of development, are furnished with cilia. 2. In the newly born mammals, and also in adult women, cilia may be found in the remains of the Wolffian body, surely in the epoöphoron. 3. The special, and perhaps normally the only, area of the Wolffian tubules which possesses cilia is the middle section. 4. The area of transition of the tubules into the main canal, namely, the outlets of the collecting tubules, as well as the main tube or Wolffian duct, are free from cilia. 5. That end of a primary kidney tubule which begins at the Malpighian body can be followed, in earliest embryonal life, beyond the capsule of Bowman up to its funnel-shaped beginning in the pleuroperitoneal epithelium. These primary kidney funnels have not been positively found to contain cilia.

Testicle.—In man the testicle receives its specific tissue elements directly from the germinal epithelium, which furnishes the primary seminal cells. The tubules which grow from the primary kidney into the testicular formation (the sexual bands) furnish an outlet to the semen. Therefore the seminal tubules, tubuli seminiferi, originate from the germinal epithelium, while the tubuli recti and rete testis originate from the primary kidney or Wolffian body. The cephalic portion of the Wolffian body forms, in addition to the tubuli recti and rete testis, the epididymis, *i.e.*, the head of the epididymis; the tail of the epididymis is formed from the beginning portion of the vas deferens. The entire vas deferens is formed by the Wolffian duct.

The lower end of the primary kidney (paroöphoron in the female) disappears. There are found for a long time in older embryos, between the vas deferens and the testicle, small twisting tubules, between which disappearing Malpighian bodies occur, and the whole forms a small yellow body. In adults the remains are quite small, forming the vasa aberrantia of the epididymis and the paradidymis of Giraldès.

The ducts of Müller disappear almost entirely in the male, but are present during embryonal life as epithelial strands. The lower ends of the ducts of Müller form the uterus masculinus. The separating wall disappears and they unite into a small tube which lies between the outlet of the vasa deferentia and the prostate. They are called "sinus prostaticus" and correspond to the vagina.

The upper end of the duct of Müller may form hydatids, small vesicles which are found upon the epididymis and are lined with ciliated cylindrical epithelium, and which may continue into a small ciliated duct. At one point they may possess a cyst-like opening. The anterior end of the duct of Müller possibly disappears in the female, and the permanent opening probably develops anew.

Just as, in the male, the epididymis tubules from the Wolffian body grow into the substance of the testicle and form the rete testis and the tubuli recti, so, in the female, *tubules may pass out from the parovarium into the medullary substance of the ovary,* and this condition is not uncommonly found in the adult.

PAROVARIAN RESTS.

Parovarian remnants are found, as a rule, on the anterior layer of the broad ligament above the enclosed parovarium, for the various parts of that ligament come from portions of the Wolffian body, and the celom epithelium of the Wolffian body becomes the peritoneum of the broad ligament. There are also found funnel-shaped pedunculated growths with their openings toward the abdominal cavity and furnished with ciliated epithelium. Two funnel-shaped openings with one pedicle also occur. Cystic remnants corresponding in position, size, and form are also found, but in place of the funnel-shaped opening a cyst is present which is always lined with ciliated epithelium.

Grape-like growths may be present. In structure they are like the above-mentioned form, but at the free edge is found a dilatation lined with ciliated epithelium.

The tubo-parovarian canal is a rudimentary canal passing off from the parovarium and lined with ciliated epithelium, which opens into the end portion of the tube, or more frequently upon the fimbria ovarica. A similar canal is found which does not open on the fimbria ovarica. It may be considered as a remnant of the Wolffian duct.

At the opening of the tube there is often found a cystic vesicle, a hydatid of Morgagni. It is a question whether it belongs to the tubules of the Wolffian body or comes from the anterior end of the duct of Müller. In the disappearance of the very first formation of the latter such a hydatid might be formed, but then a new tube opening would have to be created.

Nagel says that the main canal of the parovarium runs parallel to the tube, and that it ends blindly at its upper end, at times in a small cyst, the hydatid of Morgagni; that toward the median line it may be followed as the duct of Gartner up to the uterus. We have already mentioned that remains of it are found in the lateral walls of the body of the uterus and of the cervix, and rarely, perhaps, in the upper part of the vagina or even down to the hymen.

All these show a remarkable resemblance to the funnel-shaped remnants and the pedunculated hydatids found in the epididymis. These, too, are probably the remains of the multiple segmental communications between the Wolffian body and the celom through the medium of tubules.

I. GROWTHS ORIGINATING FROM THE PAROVARIUM (EPOÖPHORON).

(A) NORMAL ANATOMY.

The tubules of the Wolffian body have small branches, *i.e.*, microscopical lateral sprouts, which remain enclosed in the fibrous tunica propria of the tubules. The same are found in the organ of Giraldès. The tubules have large dichotomous branches, and lateral sprouts at the

blind end of the parovarian tubules. The same are present in the organ of Giraldès. The tubules of the epoöphoron are arranged in parallel order, like the teeth of a comb.

These characteristics are present in the small and large cysts originating from the parovarium.

(B) Pathological Anatomy.

(α) Small Parovarian Cysts.

These are situated at the normal location of the parovarium. They are lined with low epithelium and possess cylindrical ducts. Around them are found, microscopically, tubules lined with a low epithelium, which are twisted, varicose, branching, or with many dilatations or ampullæ and small diverticula. The ends of the tubules are frequently dilated and form cysts. Other tubules are lined with a ciliated, cylindrical epithelium. With other small parovarian cysts are found minute areas of a glandular character. These little cysts may form a continuous chain even up to the lateral wall of the uterus. The individual cysts are then usually of the size of a pin's head. Polycystomata of the epoöphoron of a diameter of fifteen to twenty millimetres may be found.

These various structures have been followed in direct continuity with uterine adenomyomata v. Recklinghausen, proving both to have developed from a common formation. In these small cysts pigment bodies may be present. In rare instances muscle fibres are found in their walls. These are usually attributed to the muscle fibres present in the broad ligament. It must not be overlooked that the parovarian tubules contain muscle fibres in their walls. The characteristics of these little cysts are a firm, fibrous wall, diverticular projections, accessory cysts, and a connection with parovarian tubules.

They are to be distinguished from lymph cysts and cysts of the serosa, both of which are lined with endothelium or a flat epithelium.

(β) Large Parovarian Cysts.

These may contain a quart or more of a clear, thin fluid, but are seldom larger than a child's head. They are intraligamentous, thin-walled, and lined in part with ciliated epithelium. They may contain a stained fluid and pigment bodies. The ovary, while usually not affected, is frequently stretched and flattened by these cysts.

Kossmann believes that most of these tumors are hydroparasalpinges. He believes that they are the result of more or less well-developed accessory tubes, especially since muscle fibres may be present in their walls, and because of the projections which may be found on their inner surface.

Accessory tubes have been found in the embryo by Nagel and several times in the sheep by Amann.

Gebhard has shown that the tubules of the epoöphoron possess a

muscularis. The muscle fibres which may be found in the wall of parovarian cysts are the result of this muscularis, or else they originate from the muscle fibres normally present in the broad ligament. By no means do all parovarian cysts possess a more or less muscular wall, which should be the case if these were developed from accessory tubes.

The projections on the inner surface may resemble the intestinal glands of Lieberkühn. These and other projections are considered by v. Recklinghausen to develop from the branches, diverticula, and lateral sprouts of the parovarian tubules. v. Recklinghausen has followed in serial sections the direct entrance of parovarian tubules into a large parovarian cyst. Klob has done the same, and Peters found this frequently in the smaller cysts, so that their origin from the parovarium (epoöphoron) is beyond question.

(γ) Adenomata and Fibroadenomata of the Epoöphoron.

Switalski, in examining serial sections of the epoöphoron in the fetus and newly-born, not infrequently found cystic formations. Minute cysts originating from these tubules were found also in the wall of a Fallopian tube, and even in the fimbria. In the mesovarium were found epithelial structures of the character of an adenoma.

Adenomata of the epoöphoron are rare. They originate from and in the normal situation of the epoöphoron. They show macroscopically and microscopically the type characteristic of the uterine adenomyomata of v. Recklinghausen. They show main tubules, collecting tubules, secreting tubules, etc. The glands are lined with simple, large cylindrical cells, often showing cilia. In addition, other glands may be present like those found in chronic hyperplastic endometritis. The glands divide dichotomously and give off cystic dilatations. This varying character of the glands is an evidence that the typical structure of the Wolffian body is not necessarily reproduced in tumors resulting from the epoöphoron. Pseudoglomeruli are also found, as well as pigment. Since these two are present also in tumors originating from the paroöphoron, a sharp distinction between the two divisions of the parovarium cannot always be drawn. Pick described a bilateral adenoma of the epoöphoron. One contained muscle fibres and much cytogenic tissue, really constituting a fibroadenoma.

(Δ) Mesonephritic Adenomata of the Ovary.

It is an interesting fact that just as the tubules of the Wolffian body enter into the testicle, forming the tubuli recti and rete testis, so do they enter into the ovary, but not as functionating tubules.

In the fox and in the newly-born female these tubules pass as the "medullary strands" enveloped in a mantle of connective tissue, from the hilus into the ovary and even up to the periphery. This "Grundstrang" is present in every ovary.

v. Franqué found, in a 20-year-old female, spaces in the ovary originating from the Wolffian body tubules. In an adenomyoma of the uterus and tube wall, Wolffian body structures have been traced in the ovary into the parenchymatous layer. An elaborate system of gland tubules and cysts has been traced from the hilus up to the ovary in a woman 54 years old. The cysts were arranged like those found in the adenomyomata of v. Recklinghausen, an especial characteristic being their tendency to dichotomous division.

In adenomata of the ovary originating from the Wolffian body tubules, we have not only cysts but adenomatous products and cytogenic tissue. The character of the cells and the arrangement of the tubules is characteristic of the tumors of v. Recklinghausen. We find tubules into which several parallel ducts empty on one side. These may be dilated at their free end. The whole form is arranged like the teeth of a comb, and such groups represent the structure of a diminutive epoöphoron. In addition, systems of tubules showing continuous dichotomous division are present. In these adenomata muscle fibres may be present. These are supposed to result from the muscle cells normally present in the ovary. It is quite possible, however, that they result from the muscular layers of the parovarian tubules. Kehrer described a multilocular ovarian cystoma whose wall contained numerous muscle fibres arranged about a system of tubules and about glands lined with ciliated epithelium. Myxomatous tissue was present in abundance. This tumor presents a proliferating glandular cystoma combined with a paroöphoral cystadeno-fibromyoma. A cystic tumor was also found in the inguinal region just outside the external inguinal ring.

Small adenomyomata, as well as the small adenomata of the ovary, may present glands resembling decidedly in structure the uterine glands. For this reason, in some instances, their origin has been attributed to cells of the ducts of Müller. From a study of our embryological review it may be seen that such an aberration is impossible.

(ε) Mesonephritic Cystomata of the Ovary (Ovarian Cysts).

(a) Simple Serous Cystoma.—These cysts are usually of the size of a child's head, usually pedunculated, yet often intraligamentous. They contain a clear fluid. The inner surface is usually lined with simple cylindrical epithelium. They are usually free from proliferating glandular structures, but not infrequently show papillary growths.

(b) Papillary Serous Cystadenoma.—These are often bilateral. The contents are serous in character. In many cases ciliated epithelium is found, in other cases none.

(c) Glandular or Papillary Pseudomucinous Cystadenoma.—The contents are a thick mucoid substance. The walls show depressions microscopically resembling the glands of Lieberkühn. These are lined with cylindrical epithelium containing very numerous beaker-like cells. The

papillary form is characterized by the presence of papillary excrescences covered by the same form of epithelium.

(d) Surface Papilloma.

(e) Grape-like Cysts which represent a transition form from *b* and *c* to *e*.

The origin of these growths has been variously referred to the epithelium of the follicles and to the germinal epithelium covering the surface of the ovary. It is impossible for the follicle epithelium to be the source of origin, for the membrana granulosa degenerates on destruction of the ovum. No one has yet observed the transition of a follicle or its epithelium into the above-mentioned growths.

The same forms of cysts occur in the male, resulting from the tubules of the testicle or from the organ of Giraldès. Since these tubules are found in the ovary, there is no question that they are the cause of the above-mentioned growths.

It is impossible that the germinal epithelium could produce such cysts, for these tumors are situated in the ovary and not so rarely intraligamentous. Even with smaller cystomata the ovarian tissue has almost disappeared, a condition not satisfactorily explained by attributing their origin to germinal epithelium. This fact can only be explained when we understand that the tubules entering from the hilus develop in all directions, and in this way involve the entire ovary. A proof of the origin of papilloma of the ovary from these tubules is seen in the fact that, in different areas of these papillomata, cysts or remnants of a cyst wall are found whose inner surface shows numerous papillary excrescences. This shows them to be papillary cystomata which have opened through and developed upon the ovarian surface.

The other forms of cystic changes in the ovary are hydrops folliculi and corpus-luteum cysts, neither of which are in genetic relation to the Wolffian body tubules.

II. GROWTHS RESULTING FROM THE PAROÖPHORON AND FROM DISPLACED REMNANTS OF THE WOLFFIAN BODY.

(A) Normal Anatomy.

An important question in proving the origin of growths from displaced remnants of the Wolffian body depends upon proving the possibility of such a displacement. Has the displacement of the Wolffian body cells been proved by examinations in the fetus?

Robert Meyer examined in serial sections the uteri and appendages of 100 fetuses, newly-born children, and older infants. v. Recklinghausen has done the same. Neither could find characteristic elements of the Wolffian body, especially in the walls of the uterus and tubes. Meyer found, however, some glands in the myometrium whose epithelium differed from that of the uterine mucosa, and one cystic gland resembling

the secreting portion of a Wolffian tubule. He believes that it will be impossible in this way to show a connection between epithelial inclusions and the Wolffian body, because such displacements naturally occur in very early embryonal life, when the differentiation of its cells has not yet taken place. There occurs, then, no displacement of glands of the Wolffian body or parts of the Wolffian duct, but only a transplantation of cells which are later on able to develop into glands and tubules, especially at puberty when the changes and stimulations of that period bring such cells to active development.

In determining the origin of tumors from displaced remnants of the paroöphoron, it is important to make a comparison between the latter and the paradidymis or organ of Giraldès. The paroöphoron is the so-called "yellow body." Although the glomeruli disappear after the fourth month, regressive glomeruli or pseudoglomeruli may be found. The tubules are of two kinds—1, twisted (secretory), and 2, straight (collecting tubule)—and possess ampullæ. v. Reckinghausen found in the tubal angles isolated glands which he considers to be remnants of the Wolffian body. Rieder found groups of cylindrical cells in the broad ligament near the lateral border of the uterus with remains of the Wolffian duct, and considers them to be remnants of the Wolffian body (paroöphoron). Ricker found a yellow body of glandular structure in the same location under the serosa. The tubules were arranged IN PARALLEL ORDER and were both straight and twisted.

In the same relative situation is found the paradidymis of the male, or the organ of Giraldès. It furnishes the vasa aberrantia of the testicle. The tubules contain cilia, but not on the flat epithelium of the glomerulus capsule. Though usually separated, they may be connected with the vasa efferentia (sexual part of Wolffian body). If so connected, they may give rise to extravaginal spermatocele. Kocher was able to inject mercury from the vas deferens into such a spermatocele, and the reverse has also been done. Injections into hydatids situated at the head of the epididymis have passed into the tubules of the epididymis, proving the former to originate from the Wolffian body tubules.

The cystomata and cystadenomata of the epididymis and testicle develop in all probability from the organ of Giraldès. The characteristics of such cysts are: 1, simple epithelium; 2, ciliated epithelium; 3, a cylindrical or cuboidal form of the cells.

The same characteristics in these and other particulars are found in the tumors mentioned below, especially in those adenomata and adenomyomata of the uterus and tube angles which v. Recklinghausen refers for their origin to the Wolffian body *i.e.*, to the distal end or paroöphoron. It may be mentioned that with those tumors v. Recklinghausen found other glands and cysts in the myometrium, undoubtedly originating from the uterine mucosa. These, however, did not contain ciliated epithelium.

The situation of certain glandular tumors in areas where glands are normally absent makes their origin from cells of the Wolffian body positive, inasmuch as embryological conditions favoring displacement are present. Therefore, even though the resulting glandular structures do not decidedly resemble those of the Wolffian body, their location is abundant proof.

Displacement of Wolffian Body Cells.

A. The inguinal band, which is first attached to the Wolffian duct and later to the duct of Müller, becomes the gubernaculum Hunteri, and finally the ligamentum teres. In this way rests of the Wolffian body may be carried into the uterine wall, into the inguinal region, or even up to the labia majora.

B. Through the change of position due to the development of the broad ligament, rests of the paroöphoron may be left in it at various points.

C. Cells of the Wolffian body may be carried into the region of the cervix by the vasa spermatica, which anastomose with the vasa uterina, or by the duct of Gärtner.

D. Some of the cells of the Wolffian body may be left on the posterior abdominal wall.

E. Through the spiral twist of the ducts of Müller and the distal continuation of the Wolffian body, the dorsal side of the uterine portion of each duct of Müller lies upon the lower end of the Wolffian body and may take up some of its cells.

(B) Pathological Anatomy.

Ad A. (*a*) Fibroadenoma of the Ligamentum Teres.

The cystic tumors of the round ligament are either hematomata or else constitute a hydrocele (canal of Nuck). The solid tumors are either sarcoma, sarcoadenoma, or cystofibroma. The latter may be situated in the round ligament within the abdomen, subcutaneously and external to the inguinal ring, or within the inguinal ring, breaking through all the tissues of the abdominal wall. In adenomata of the round ligaments may be found muscle tissue, and certainly fibrous connective tissue. Islands of glands and cysts are present. The glands show prominences made up of cytogenic tissue, which are called "pseudoglomeruli." The epithelium is simple, cuboidal, or cylindrical, but may be flat like endothelium. The cysts and ampullæ are filled with blood, pigment, red blood cells, leucocytes, cell detritus, or hyaline substance. They show the characteristics of v. Recklinghausen's adenomyomata, to be mentioned later.

Although these glandular structures do not always decidedly resemble in form and structure the Wolffian tubules, yet they undoubtedly originate from epithelial cells of this organ. In some cases the glands

bear a decided resemblance to those of the uterine mucosa. It must be mentioned that adenomata of the epoöphoron itself contain glands lined with simple cylindrical epithelium, often ciliated, while other glands are present resembling those found in hyperplastic endometritis.

The inguinal band is connected only superficially with the duct of Müller, and as the epithelium of the latter is not near the surface none of its cells can be carried along. The glands of the Wolffian body, however, are connected with the celom epithelium, and thus some of their cells may be transplanted by the inguinal band to any point of the subsequent situation of the ligamentum teres.

Ad B. (β) Paroöphoral Cysts of the Broad Ligament.

Such cysts may be present in the various parts of the broad ligament and yet the ovary and the epoöphoron are present. Cysts originating from the epoöphoron usually contain a clear fluid, are thin-walled and lined with cubical, cylindrical, and also ciliated epithelium. Cysts originating from the paroöphoron, because of the pigment characteristic of this portion of the Wolffian body, usually contain a brownish fluid and pigment in the cellular tissue of the wall. They are lined with cubical or cylindrical epithelium, and cilia may be found in the cells of the wall or in cells of the contents. The latter contains large pigment bodies with a pigmented protoplasm and dark brown nucleus. They are usually situated near the lateral border of the uterus.

(γ) Cystomyomata of the Broad Ligament.

Such tumors not connected with the uterus have frequently been explained as being tumors originating in the uterus and connected with it by a pedicle. On the disappearance of the pedicle the tumor was considered, therefore, to have originated from the uterine structure.

Other tumors of this character have been considered as developing from the muscular tissue in the broad ligament, and the cystic areas have been attributed to softening and degeneration, or to dilatation of lymph spaces or tissue spaces. Even though most previous descriptions have made but rare mention of the presence of glands, close examination would probably find such to be present in many instances, if not in all. If such glands are present, their origin must be attributed to cells or rests of the Wolffian body, namely, of the distal portion, the paroöphoron. It has already been mentioned that in descent of the adnexa, and the change of position and development of the broad ligament, such cells and rests may be carried along. These tumors have been found to contain ciliated epithelium and a brownish, thick fluid, The primary tumors of the broad ligament (desmoid tumors) include also sarcoma, cystosarcoma, chondrosarcoma, etc. It is perfectly possible that these have developed from mesodermal cells displaced into the broad ligament by the inguinal band or by the paroöphoron. In that event the glandular

elements have either not been found or have disappeared, or else mesodermal cells alone have been displaced (see Cytogenic Tissue).

Ad C. (Δ) Adenomata and Fibromata of the Cervix.

Such tumors have been found on the dorsum of the cervix and in the posterior fornix. In the lateral wall of the cervix they may result from the root-like extensions of the duct of Gartner, or from rests of the Wolffian body displaced by the duct of Gartner or by the vasa spermatica. Fibromyomata in the posterior fornix extending from the muscle wall of the vagina into the paravaginal tissue have been described. If glands are present in such tumors they constitute adenomyomata. A situation on the dorsum of the cervix speaks in favor of an origin from rests of the Wolffian body. A characteristic of fornical adenomyomata is the dichotomous division of the tubules.

Ad D. (ε) Adenomata and Cystadenomata of the Posterior Abdominal Wall.

In the descent of the parovarium from the posterior abdominal wall into the broad ligament elements may be left behind giving rise later to pathological growths. Hartz described a cystadenoma on the posterior abdominal wall containing cysts and glands with the characteristic structure of the Wolffian body tubules as well as glomeruli. The genitalia were entirely intact and the growth was not possibly related to the duct of Müller. Although undoubtedly a derivative of the Wolffian body or its cells, many of the glands and cysts bore no resemblance to the tubules of the mesonephros. Cytogenic tissue was present in large amount.

Ad E. (ζ) Glands and Cysts in the Myometrium.

Deep branches of the mucosa frequently extend into the muscular wall of the fundus of the uterus and the tubal corners. With adenomata such glands and cysts in the myometrium may be separated parts of the same. If not situated far from the mucosa they are to be considered as post-fetal growths of the latter. If, however, they are situated far from the mucosa or near the serosa, they are to be viewed as congenital displacements either of cells of the duct of Müller or of cells of the Wolffian body. A positive distinction cannot be made from their form and structure. Pick found in the external muscle layers of the posterior wall of the uterus small numbers of isolated scattered glands, not connected with the mucosa. Because of the presence of a typical lymphadenoid stroma, he believes them to have originated from cells of the ducts of Müller (see Cytogenic Tissue).

(η) Subserous Glands of the Uterus.

These occur more frequently than is generally known. They are situated, as a rule, anteriorly or posteriorly, or both, and never laterally.

They are found, as a rule, in the lower part of the uterus, and are lined with an epithelium almost like endothelium. They generally occur in the subserous longitudinal muscle layer. As to their origin various possibilities are to be taken into consideration:

1. Displaced cells of the ducts of Müller. Since these glands are usually subserous and often communicate with the peritoneum, such an origin is not probable.

2. A post-fetal origin from the mucosa is improbable because of their situation.

3. An origin from the serous membrane itself, either congenital or acquired, especially the latter, is probable because such glands are not found in the fetus, and probably develop later with peritoneal irritation. Meyer believes that the endothelium of the serosa changing to epithelium is the cause of most of these glands. Since a change of serosa to ciliated epithelium has not yet been observed, this view is probably incorrect for all cysts or glands lined with anything but endothelium, and displaced cells of the Wolffian body are the most probable cause. This is especially probable if the glands show a papillary structure and club-shaped epithelium. Cells of the Wolffian body or of the germinal epithelium may be displaced into the serosa and develop later. Pick described a cystadenoma of the ovary with a ciliated cyst containing glands on the parietal peritoneum. Papillary excrescences were likewise found. Since the same structures were found in the subserosa, the Wolffian body or its cells are the probable source of origin of the entire group. The situation of such glands speaks against their origin from the duct of Gartner, for the latter is situated in the lateral border of the perimetrium or uterus. With malignant adenoma of the uterus it is possible that such glands may be present in the serosa as metastases.

(9) Retrouterine Subperitoneal Cystomata.

Pfannenstiel described subserous cysts lined with simple ciliated epithelium and situated on the posterior wall of the uterus. On the lateral wall were several small cysts, also lined with ciliated epithelium. v. Recklinghausen found in conjunction with adenomyomata of the uterus polycystomata in the sac of Douglas and small subserous cysts on the fundus. Their structure brings them into the class of adenocystomata. A case of Döderlein's was composed of cysts of the character of ovarian cystomata with papillary excrescences. In addition was found a hard appendage composed of smooth muscle fibres.

Krönig described a polycystoma originating in the uterus and growing into the sac of Douglas and extending up to the umbilicus. Both adnexa were normal, as were also the broad ligaments. The area at the base of Douglas' cul-de-sac had the structure of a cystic adenomyoma with an arrangement of glands typical of the tumors of v. Recklinghausen. Pigment, hemorrhages, and pseudoglomeruli were present,

making the diagnosis one of paroöphoral myoma. The cystic portions were made up of glands and cysts lined with simple cylindrical epithelium and contained a brownish-red fluid. Numerous muscle fibres were present in the wall of the cystoma.

(ι) Adenomata of the Tubal Angles.

That portion of the tubal canal which lies in the uterine wall is called "pars uterina." The greater portion of the pars uterina towards the fundus uteri has glands in its mucosa and really belongs to the uterus, being called the "tubal corner." The really interstitial part of the tube possesses its own muscularis and has no glands in the mucosa, and is called the "tubal angle." In the tubal corners a congenital branching of the mucosa is frequent, and the majority of adenomatous areas are probably acquired, occurring in the tubal corners more frequently than in the myometrium.

In the "tubal angles," however, adenomata appear usually in the external layers, but may be found in all layers of the muscularis. They may communicate with the lumen, but rarely with the serosa. The glands may be found scattered or closely grouped, usually scattered. There is often found a "system" of tubules entering into a central reservoir called the "ampulla." The tubules are lined with simple cylindrical epithelium, the cells and nuclei being arranged in even line. The ampullæ have a high epithelium on the floor and a low epithelium on their roof. These adenomata often communicate with the mucosa. The epithelium, however, which lines the communicating tubules is quite different from that of the mucosa, for the latter may be arranged in two layers and the nuclei and cells form an irregular line. Although the mucosa of the tubal angles may be the source of adenomata, the characteristic structure of the large number of adenomata of the interstitial portion, and the character of the epithelium lining the tubules communicating with the mucosa, make the origin of such adenomata from the Wolffian body highly probable.

(κ) Adenomyomata of the Uterus and Tubal Angles.

In adenomyomata of the uterus and tube, whose origin he refers to displaced cells of the Wolffian body, v. Recklinghausen distinguishes (1) the larger forms, which are found in all layers of the myometrium, and (2) the smaller ones, which are found especially in the peripheral layers of the uterus and the tube. In contradistinction to other myomata which are well outlined and can be frequently shelled out, these adenomyomata are characterized by their tendency to infiltrate the surrounding tissue. v. Recklinghausen distinguishes the following forms in the uterus: 1. The hard form, with more muscle than adenomatous tissue. These are generally situated in the peripheral part of the uterus. 2. The cystic form, with macroscopic spaces and cysts. 3. The softer

form, with much adenomatous tissue, and islands of glands embedded in cytogenic tissue. 4. The softest form, with vascular and almost cystless adenomatous tissue, the so-called "angiomatous form."

These adenomata of the corpus uteri are almost always found on the dorsal wall. They grow (1) from isolated centres, forming large masses, generally in the periphery, or (2) from numerous centres, extending therefore in the various layers of the muscular wall.

Such adenomyomata are to be distinguished from myomata containing cysts due to softening of myomatous tissue, or to a dilatation of tissue spaces, or to a dilatation of lymph vessels, in which event they are lined with endothelium.

The glands in these tumors of the uterus are usually "closely grouped." The myomatous portion of the tumor seems then to grow independently of the glandular, and the individual tubules of the glands have no muscle boundary. Yet the myomatous elements somewhat distinctly outline the adenomyoma from the surrounding tissue. There is often, in addition, a real hypertrophy of the entire myometrium, due probably to the stimulations of puberty, which make such an hypertrophy independent of the stimulation due to the adenomatous formation. In all the tumors described by v. Recklinghausen the patients were over twenty years of age. Large tumors with much muscle tissue were found in women up to the fifty-sixth year; none were found in recently gravid uteri.

In the smaller tumors of the uterus, especially if the glands are "scattered," the muscular constituents grow hand in hand with, and proportional to, the adenomatous growth and about the individual ducts.

The majority of the adenomyomata of the tube are bilateral and occur usually in the tubal angles. v. Recklinghausen finds them on the dorsal wall and on the cranial side of the interstitial portion, but sometimes about the tube. They are of two forms, (1) the hard form, with a close grouping of fibrous and muscular tissue and the presence of tense cysts; (2) the soft form, which has a red appearance on account of the numerous blood vessels, and which is almost angiomatous. The hard form contains very little cytogenic tissue, but the soft form contains relatively much more. The glands are usually arranged in "scattered" order and evidence a decided tendency to the formation of cysts. The cysts are branched, sending out ducts lined with a somewhat higher cylindrical epithelium. The muscle fibres form a boundary about the individual tubules, in a longitudinal direction, and their growth goes hand in hand with, and proportional to, the development of the adenomatous areas. The same is true of those tumors of the uterine wall which are small and contain "scattered" glands. These adenomyomata are more frequent in the tubal angles than in the uterus.

The characteristic element in these adenomyomata is furnished by glands lined with simple cylindrical (ciliated) epithelium. In this

respect they resemble the Wolffian body. Ciliated epithelium is normally present in the Wolffian body tubules, and in many growths resulting from them, such as (1) cystomata and cystic fibromata in the hilus of the ovary, (2) parovarian cysts and ovarian cystomata genetically related to the Wolffian body, (3) cystic myofibromata in the broad ligament, (4) cysts and parovarian rests in the ala vespertilionis, (5) paroöphoral cysts, (6) subserous and retrouterine adeno-cysts, (7) like growths of the organ of Giraldès. Cilia have been found in the adenomyoma of an eighty-two-year-old patient.

v. Recklinghausen distinguishes in these tumors (1) narrow tubules lined with a high epithelium, called "collecting tubules"; (2) wide twisting ducts with a lower pale cylindrical epithelium, called "secreting tubules"; (3) wide, blind ends lined with a flat epithelium; (4) dilatations called "ampullæ," which are divided into *(a)* main or large ampullæ, into which empty the collecting tubules in parallel order like a comb, and always on one side, *(b)* ampullæ at the end of a tubule, and *(c)* ampullæ in the course of a tubule.

In this respect they resemble the Wolffian body. The tubules of the Wolffian body have dichotomous branches, and lateral branches are found in the blind ends of the parovarian tubules and in the organ of Giraldès. In the parovarian tubules of the adult woman are found microscopically short, lateral sprouts which remain enclosed in the fibrous tunica propria of the tubules. It is from these that the small and large dilatations at the ends of the tubules and in the course of the tubules develop in these tumors. In every microscopical group of gland ducts in these tumors the comb form is a characteristic. In this respect there is a further resemblance to the Wolffian body or parovarium.

While resembling in these details the parovarium, their origin is attributed to the distal end, or paroöphoron, because of the presence (1) of pseudoglomeruli and (2) of pigment bodies. The pseudoglomeruli are round or semicircular elevations of cytogenic tissue in the ampullæ. They differ, however, from the Malpighian bodies in that they contain no vessel knots and in being covered with cylindrical epithelium (flat epithelium in the Malpighian body). Yet their structure, says v. Recklinghausen, proves them to be incomplete glomeruli. The pigment found in these adenomyomata consists of *(a)* large "pigment bodies" in the lumen of the ducts, *(b)* oval or many-sided pigmented cells in the tissues, *(c)* pigmented cells arranged in mosaic. Pigment is a characteristic of the paroöphoron and the organ of Giraldès, and these "pigment bodies" are found in the previously mentioned cysts and tumors originating from the paroöphoron.

A further proof that these glands owe their origin to the paroöphoron is found in the fact that the organ of Giraldès has branched tubules, various forms of cylindrical epithelium, ciliated epithelium, varicose

dilatations of the lumina, cyst formations, pigment bodies, and glomerulus-like structures. A further proof is found in the fact that the adenomata and cystadenomata of the testicle, due in all probability to the organ of Giraldès, have the same dilated form of cysts, gland ducts entering into cysts, simple cylindrical epithelium, and ciliated epithelium.

For these reasons, and because of their characteristic structure, v. Recklinghausen considers that these adenomyomata of the uterus and tubal angles result from cells or rests of the Wolffian body, especially of the distal end, the paroöphoron. In many areas, however, the glands do not resemble closely the form and structure of the Wolffian body tubules. They differ from the latter further in that they possess no tunica, as is the case with the tubules of the Wolffian body and with Bowman's capsule. In addition the Wolffian body tubules are not embedded in cytogenic tissue. However, the situation of these tumors on the dorsal wall of the uterus and in the tubal angles is characteristic, and is explained by the fact that it is these parts of the ducts of Müller which, *in making their spiral twist,* lie with their dorsal wall upon the Wolffian ducts and the lower end of the Wolffian body, a condition which makes a displacement of cells of the latter easily possible. Further, near the tubal angles are inserted the round ligament, the broad ligament, and the ovarian ligament.

It has recently been claimed that the mucosa of the uterus and tube is the origin of these adenomyomata. From a study of the adenomata of the uterus and tubal angles there is no question that in many instances such is the case. The difficulty is that the structure of the adenomatous areas is by no means always characteristic. The displaced cells of the Wolffian body develop years after their transplantation and must not necessarily form the characteristic divisions of the original Wolffian body tubules. We have seen that in adenomata of the posterior abdominal wall and in adenomata of the ligamentum teres, and also, as will be seen later in adenomata of the parovarium, the glands are by no means characteristic, but may frequently resemble the form and structure of the uterine glands.

The important point must then be the *resemblance of these adenomyomata to other growths developing from Wolffian body cells.* It is this fact which makes the subsequent determination of the origin of glands and cysts difficult and often impossible. Even the presence of cytogenic tissue is no absolute proof of an origin from Wolffian body tubules.

v. Recklinghausen believes that the following characteristics speak for his theory: (1) The location of these tumors does not correspond to the entire length of the duct of Müller or of the Wolffian body, but represents only that point where the *duct of Müller crosses the duct of Wolff.* (2) The situation of these tumors is so frequently peripheral. (3) Through their peripheral situation they frequently grow

into the subserous and parametrial tissue. (4) Even though they may grow toward and close to the mucosa, the centres of such tumors are usually peripheral. (5) Such tumors are almost never found in the cervix. (6) The interstitial portion of the tube, which is so frequently the seat of these adenomyomata, possesses no glands in the mucosa.

It must be mentioned that examinations have proved the fundus and tubal corners to be especially disposed to the formation of adenomata. A peripheral situation does not necessarily speak against a fetal displacement of cells of the ducts of Müller. The interstitial portion of the tube, though possessing no glands, has nevertheless been proven to be the seat of adenomata of the mucosa. For these reasons, unless adenomyomata show glands quite characteristic of the Wolffian body tubules, their origin, in the uterus, is to be referred to the mucosa.

In the tubal angles, however, it is probable that because of their frequently characteristic structure the majority of adenomyomata are to be referred to the Wolffian body.

Adenomata of the Uterus and the Tubal Corners Originating from the Mucosa.

A decided growth of mucosa into the myometrium must be viewed as adenoma. The growths often form microscopic areas, consisting of hyperplastic glands with a stroma rich in spindle cells. The growth extends into the muscle interstices, often along the lymph channels, and is accompanied by connective tissue. The vessels often show hyaline degeneration, sometimes arteriosclerosis, and are often varicose and dilated.

The adenomatous growths are most frequently found at the fundus and in the tubal corners, especially in the latter. A preference is shown for the inner and middle muscular layers. The middle third of the corpus is usually less affected than the fundus. The lower third is, in comparison, little affected, the cervix very rarely.

This adenomatous condition is not always in continuity, but is generally scattered over the mucosa. Long tubules are found in the muscle interstices and along the lymph spaces, or else complexes are scattered through the muscle wall with branches and cysts. The glands at the periphery are often cystic. Numerous short dilatations are found at short intervals in the course of the tubules, giving a grape-like appearance, often pointing to beginning malignant degeneration. The cysts in the fundus and tubal corners are often large, giving off vesicles. The structure of these formations is characterized by the *absence of any special system.*

The epithelium is simple high cylindrical, with irregularly placed nuclei. The connective tissue consists of closely grouped spindle cells, and their growth is usually in advance of the glands. Connected with

chronic interstitial and atrophic endometritis there is more connective tissue than glands. The muscle wall is but slightly hyperplastic.

The fundus of the uterus shows a special disposition to the entrance of the hyperplastic mucosa into the muscle wall, and therefore to adenomata and to adenomyomata. Adenomata, as seen above, may exist in the myometrium without the presence or formation of myomata. The deeper parts of the adenomata easily become malignant, and many cases of adenomatous growths are probably transitions to carcinoma.

Adenomyomata of the Uterus and Tubal Corners Originating from the Mucosa.

These may be congenital and due to a fetal displacement of cells of the ducts of Müller or to a post-fetal growth of mucosa. The latter origin is proven by the occurrence of lower and higher grades of hyperplasia of the mucosa in the upper part of the corpus uteri and tubal corners. It is beyond question that most of the uterine adenomyomata originate from the mucosa. Their frequent occurrence at the fundus and in the tubal corners is explained by the fact that this situation represents the highest point of union of the ducts of Müller. The disappearance of the intervening wall and the formation of the fundus is an irregular and complicated process giving abundant opportunity for various degrees of cell displacement. The origin from the mucosa is now acknowledged even for numerous cases previously attributed to the Wolffian body.

v. Recklinghausen considers the following characteristics to be proof of origin from the mucosa: (1) A situation in any portion of the uterus other than the dorsal wall and the tubal angles. (2) A development from the central or inner layers of the myometrium. (3) A close apposition of the tumor to the mucosa in the greater portion of its extent. (4) Numerous communications with the mucosa. (5) A tendency to surround the uterine cavity in its entire circumference. (6) The absence of special characteristics in the structure of the glandular portions of the adenomyoma.

It may be said that a position on the ventral wall of the uterus speaks almost positively for an origin from the mucosa. A situation in the peripheral layers of the uterine wall does not necessarily speak against such an origin, for cells of the ducts of Müller may be displaced peripherally.

Doubtful Cases.

It is claimed that the mucosa of the tubal angles is capable of forming glandular structures showing the characteristics believed to belong only to those growths originating from the Wolffian body.

Salpingitis Nodosa Isthmica.

v. Franqué described this condition. The thickenings are due to groups of muscle tissue enclosing various epithelial structures. The groups are usually in the periphery, and in this case tubercles were found. The tubules are lined with cylindrical epithelium ciliated in parts, and cytogenic tissue is also present. Glands are found in all layers of the tube wall and, in the less affected areas, near the mucosa.

Although the glandular structures possess the characteristics mentioned by v. Recklinghausen, the mucosa of the tube is considered to be the source of origin *because of the multiple connections between the glands of the adenomyoma and the tubal mucosa.* The peripheral situation of many of these structures is explained by a separation of the glands from the lumen of the tube through growth of the intervening muscle fibres.

Gottschalk described an intraligamentous cyst in the mesosalpinx composed of multiple cysts, some as large as an orange. In the wall of the tube, and extending into these cysts, were found glands lined with simple cylindrical ciliated epithelium as in the case of v. Franqué. At numerous points were found *direct communications between these glands and the tube lumen,* and for this reason the origin of the entire growth is referred to the tubal mucosa. No cytogenic tissue, however, was found.

Opitz found under the serosa of the uterus several small myomata. In the isthmus tubæ of both sides were found several adenomyomata with the typical structures mentioned by v. Recklinghausen. Many direct communications between the glands and the tube lumen were found, and the origin of these adenomyomata is therefore referred by him to the tubal mucosa.

The communications between the adenomata and the mucosa of the uterus and tube may, however, be explained as follows: (1) The glands, probably derivatives of the Wolffian body, in their growth and extension may naturally open into the mucosa. (2) This is especially probable in the interstitial part of the tube, because normally its mucosa has no glands. (3) The cells of the Wolffian body which have been displaced become attached to the duct of Müller (the future mucosa of the uterus and tube), and may thus lie near the inner surface of the uterus or tube after mesoderm has formed their muscular wall. (4) An abnormal union may take place between the ducts of Müller and the displaced cells of the tubules of the Wolffian body, and a continuation of this union constitutes, after development of the tubules and glands of the adenomyoma, a communication between them and the uterine or tubal mucosa.

The origin of adenomyomata in the tubal angles at least, is probably, in the majority of cases, the result of a displacement of Wolffian body cells, because they are found in the periphery, and because glands are absent in the interstitial portion. In addition, the glands often show the

typical Wolffian body structure, and their epithelium is quite different from that of the tubal mucosa. As to the communications, these probably result from the glands of the adenomyoma, especially if the epithelium of the communicating tubules differs from that of the tubal mucosa. The epithelial cells are of equal height, with nuclei arranged in an even line, while the epithelium of the tubal mucosa is often stratified and quite irregular. In addition, the communicating tubules often possess a muscularis.

The present view is the following: (1) Adenomyomata of the uterus—the majority originate from the mucosa. Those situated dorsally and peripherally, if the structure is absolutely characteristic, probably originate from Wolffian body cells. (2) Adenomyomata of the tubal corners originate from the mucosa (the majority) or from the Wolffian body. (3) Adenomyomata of the tubal angles may originate from the mucosa, even though glandless, but the majority are to be referred to the Wolffian body.

Cytogenic Tissue.

This tissue is usually present in those adenomyomata of the uterus and tubal angles whose origin has been referred to the Wolffian body. It is a reticular lymphadenoid tissue with a basis consisting of a delicate reticulum with closely grouped, small, flat, spindle and star-shaped, but especially round cells. It is found normally in organs possessing numerous glands and going through numerous epithelial changes, such as the uterus and the intestine. It is possible that the regeneration of the uterine epithelium and glands is performed by these cells, inasmuch as the large epithelial-like cells of the decidua result from these round cells.

v. Recklinghausen believes that the cytogenic tissue results from a hyperplasia of connective tissue. Meyer believes it to be the result of an increase in the number of cells and vessels of the paroöphoron, while others consider it to be developing muscle tissue.

Pick considers the cytogenic tissue which forms the stroma of the uterus to be like lymphatic tissue found elsewhere in the body, and Leopold considers the uterus to be simply a large lymph gland. Pick says that this tissue is not normally present in the rests of the Wolffian body and the Wolffian duct, but only develops as the stroma of the tubules when the Wolffian body tubules develop in large amounts. Therefore, if there is only a slight development of the tubules, or if they are scattered as in the tubal angles, no cytogenic tissue is found, for its production goes hand in hand with the growth and activity of the glands.

This question is of importance in determining the origin of glandular structures found in the myometrium. Pick, finding such glands in the dorsum of the uterus, attributed their origin to the uterine mucosa because, in spite of a slight growth of glands, much cytogenic tissue was present.

On the other hand, according to Hartz, the presence of cytogenic tissue, whether there is great or slight development of glands, is an evidence of the presence of embryonal tissue which is either already differentiated or is still capable of further differentiation. He believes that cells are present in the epoöphoron and paroöphoron which have the power to proliferate and also to form cytogenic tissue. These round cells are then at a certain stage already differentiated embryonal cells lying in a fine meshwork of connective-tissue fibres. At another earlier stage they may be capable of further differentiation and are to produce epithelium, glands, and connective tissue.

It is a fact that it is difficult to state what tissues are to result from the various blastodermic layers in the early embryonal period. For instance, the cells of the mesoderm form connective tissue, muscle, bone, cartilage, etc., yet before the stage of differentiation the future of any group of cells cannot be determined by their form. For this same reason, displaced cells of the Wolffian body cannot be found or recognized in the uterine wall of the fetus and the newly-born, for they are then only embryonal cells which later on may form the characteristic structures of the Wolffian body. When, therefore, in the future development of such displaced cells of the Wolffian body, round cells and other cells of cytogenic tissue are found, these may be either embryonal cells destined to form new glands and cysts, or else they are already differentiated into permanent connective-tissue cells.

As this cytogenic tissue is normally present in the uterus, its presence in pathological glandular growths cannot be viewed as proof either of an origin from the Wolffian body tubules or of an origin from the uterine mucosa. It must be stated, however, that in tumors of the epoöphoron, and in adenomata of the ovary originating from epoöphoron tubules, cytogenic tissue is present. In myomata of the corpus uteri islands of cytogenic tissue are also present without epithelial elements. Here either the latter have degenerated or else simply the stroma of the mucosa has been displaced without epithelial cells. This is of interest in explaining the desmoid tumors of the broad ligament, for in many of these glandular elements are not present. These mesodermal tumors may be then simply mesodermal cells displaced with or without the aid of the paroöphoron. In the former event the epithelial elements may have disappeared.

III. DUCT OF GARTNER AND GROWTHS ORIGINATING FROM IT.

(A) Normal Anatomy.

Robert Meyer found this duct in all fetuses of two to three months, in 28 per cent. of fetuses of four to six months, and in those of seven to

nine months in 16 per cent., frequently on both sides. In the newly-born it is found in 16 per cent. In children it was followed twice into the vagina. In adults, as in the fetus and in children, its remnants are found in the supravaginal part of the cervix.

Its situation is originally in the lateral border of the uterus. In the cervix it takes a more mesial course, lying in the lower part of the supravaginal portion very close to the cervical mucosa. Further down, in the upper part of the vaginal portion of the cervix, it again lies more laterally. It is rarely found in adults in an uninterrupted course. It enters into the uterus at the lower part of the body both in children and in adults. In rare cases it may be traced from the fundus down. Its situation varies in that it may in different cases be more lateral or less external, or situated more or less anteriorly or posteriorly, usually more anteriorly. Although usually taking a straight course, it is sometimes twisted.

In the fetus and in children it is a narrow cylindrical canal with branches, the canal becoming wider and more flattened in its own downward course. The dilated section in the cervix is called the "ampulla." Its walls present branches which pass into real glands. In adults it is present as remnants showing cystic degeneration, the main canal being rarely visible. The walls of the ampulla are smooth, but show projections. From the ampullæ extend wide branches or narrow tubules which run into straight or twisted glands. The glands are more numerous than in the fetus and in children, and occur in adenomatous bands, usually grouped about the main lumen, and may extend up to the mucosa and through the middle muscle layer.

The epithelium of the duct of Gartner in the fetus and in children is simple cylindrical with a long nucleus. The cells stain well and show the same character in adults. The branches are lined with low epithelium. The narrow tubules have the lowest cubical epithelium. These stain poorly and are often overlooked. The epithelium, as mentioned, is usually simple, though in pathological conditions it may be stratified.

The duct of Gartner possesses a muscularis as a layer only in its upper part. This is sometimes, but rarely, arranged in three layers, circular and longitudinal. Generally a circular layer with a slight external longitudinal layer is present. This is sometimes quite sharply outlined from the myometrium, taking the stain better than the latter. In the vaginal portion of the cervix the muscularis is absent.

The ampulla of the duct of Gartner in the fetus and in children is homologous with the pars ampullaris of the vas deferens. The glandular formations are hyperplastic. In adults they may cause adenomata and carcinomata.

Koeberle found the duct of Gartner opening into the cervix at the level of the internal os of a one-horned uterus. Passable for a bristle, it was traced upward for a distance of 35 mm., whence it continued fur-

ther on to the parovarium. It was lined with a mucosa of simple cubical epithelium. In a uterus bipartitus with vagina septa and atresia of right vagina, Koeberle found the duct of Gartner opening into the right vagina. Klein traced the duct of Gartner in a newly-born infant from the right parovarium through the broad ligament, through the uterus and vagina, up to the hymen, with but one slight interruption. Baudelocque traced the duct of Gartner parallel to the uterine cavity from the intramural tube to the internal os, into which it opened.

v. Recklinghausen finds that in adults remains of the duct of Gartner are generally preserved in the cervix as a fibrous or muscular cord. Sometimes a lumen lined with cylindrical epithelium is present. At times glands are found. In other uteri are found cytogenic tissue and glands, and in others simply islands of lumina lined with cylindrical epithelium.

The part distal to the ampulla is homologous with the ejaculatory duct of the male. The ampulla develops at about the seventh month of fetal life.

(B) Pathological Anatomy.

(α) Cysts of the Duct of Gartner in the Parametrium. (See Vaginal Cysts.)

(β) Cervical Cysts of Gartner's Ducts.

These may be due to (1) post-fetal displacement of cervix mucosa, (2) to post-fetal displacement of cervix mucosa associated with cystic endocervicitis, (3) to mucosa implanted in cervical lacerations, (4) to a communication of cysts of the duct of Gartner with cysts of the mucosa, forming mixed cysts, (5) to products of the duct of Gartner or its branches.

Small cysts are found in the fetus and in children. It is difficult to distinguish these from cysts of the cervical mucosa, especially as these cysts and those of the cervix may communicate, forming mixed cysts.

(a) Small Cysts.

Cysts of a diameter up to two millimetres are found in adults. They are of irregular shape and twisted, arranged in rosettes. Their epithelial cells are of varying heights.

(b) Large Cysts.

These displace the cervical tissue, especially in the lateral wall. In these the epithelium is so changed that it is difficult to tell whether the cysts originate from the duct of Gartner or from the mucosa. They are cysts of two to ten millimetres diameter, lined with low epithelium, rarely with cylindrical. The muscle fibres, especially about the larger cysts, are partly arranged in a circular manner. Those cysts not origin-

ating from the duct of Gartner are distinguished by the crossed course of the muscle fibres in their wall, thus differing from the tunica of the duct of Gartner. The contents of these cysts are composed of nuclei, leucocytes, mucus, and fibrin.

(γ) Adenomata and Adenocystomata of the Duct of Gartner.

Such growths occur in the cervix and fornix. A decided location on the dorsum of the cervix or fornix of the vagina, however, speaks for an origin from the Wolffian body.

Adenomata at the sides of the cervix or vagina are probably developed from the duct of Gartner. With adenomyomata of the tube angles there has been found in one case a small cervical cystadenoma, in another case an adenocystoma of the duct of Gartner.

(Δ) Adenomatous Hyperplasia of the Cervical Gland Appendage of the Duct of Gartner.

This condition involves both the vaginal portion and the rest of the cervix, and is evidenced clinically by a soft, friable vaginal portio. The duct of Gartner is found lined with low, simple epithelium giving off long, dividing tubules, often twisting and turning, and lined with simple cubical and short cylindrical epithelium. These extend into the vaginal portion of the cervix and break into the muscularis.

VAGINAL CYSTS.

(A) Normal Anatomy.

In the fornix and upper part of the vagina the duct is situated laterally and somewhat anteriorly. Further down it is situated more laterally. In its course through the vagina it lies quite near the mucosa. That the situation varies somewhat may be seen from the fact that Meyer traced the duct of Gartner up to the hymen, finding it at first situated laterally, and then taking a more anterior course, and finally running more posteriorly into the middle of the lateral wall of the hymen up to its anterior layer. In the lower two-thirds it is generally lateral or antero-lateral. The duct of Gartner has been found to be lined even with two layers of epithelium in various portions of the vagina. A tunica of muscle fibres is rarely present. Cilia have not yet been found in the duct of Gartner in the human being, but Rieder believes that the epithelium may be ciliated.

Meyer, after examining 60 fetuses and newly-born, comes to the following conclusion concerning the glands of the vagina:

Glands of the vagina are found: 1. Isolated in one-third of the cases. These are referred to a failure on the part of the projections formed in the first half of fetal life to develop into squamous epithelium.

2. Glands develop in the last months of fetal life from the basal stratum of the developed squamous epithelium.

3. Epithelial heteroplasia from the cervix above, or vestibule below, occurs less frequently and appears as glandular islands or evidences itself through formation of mucous glands. Glands in the vaginal wall without connection with the mucosa belong to the vestibule or Wolffian duct or Wolffian body. The opening of the Wolffian duct is generally in the hymen, in which it runs up to the free edge anteriorly. The squamous epithelium of the Wolffian duct before its opening belongs to the external layer of the hymen. This epithelium may be present on any side or may be quite absent. Glands of the Wolffian body have been found in one case in the upper part of the vagina. Anteriorly they were within the circular vaginal muscular layer; posteriorly external to it up to the pararectal connective tissue. They resemble the tubules of the Wolffian body.

(B) Pathological Anatomy.

The origin of vaginal cysts has been variously referred to the following sources: 1. The duct of Gartner. 2. Cells or rests of the Wolffian body. 3. The glandular branches of the ducts of Gartner. 4. The real (?) glands of the vagina. 5. Double rudimentary vagina. 6. Union of vaginal folds. 7. Lymphectasiæ. 8. Edema and exudations or serous traumatic exudations. 9. Accessory ureters. 10. Echinococci.

Abel, Nagel, Gebhard, and Waldeyer have never found glands in the vagina. Veith and Testut say that the vaginal glands of the lower portion of the vagina are displaced aberrant glands of the sebaceous glands of the vulva or of the glands of Bartholini.

Cysts are found lined with cylindrical epithelium, with squamous epithelium, or with both, depending upon whether they develop from the body or from the ducts of the so-called vaginal glands. This is the view of those who believe that glands of the vagina may be present.

Davidsohn found at the highest point of the right fornix, and descending along the posterior vaginal wall of the middle of the vagina, a series of irregular prominences like a cock's comb, each the size of a pea or smaller. The whole extended over an area of three to four centimetres. In the submucous connective tissue were glands with cystic spaces lined with epithelium and often showing papillæ. At many points there was a decided resemblance to the glands of the cervix, while in other areas the epithelium was cubical or flat. No cilia were found. These cystic spaces were situated in all layers of the submucosa, but did not extend into the muscle layer. A frequent connection between the glands and cysts and the surface or lining of the vagina was noted. The cylindrical epithelium in the ducts of communication showed transition into the squamous epithelium of the vagina. Numerous transitions from glands to cysts were noted.

For this reason and for the following reasons the origin of this condition was attributed to vaginal glands: 1. Because the cysts are multiple and of small size. 2. Because the epithelium is simple. 3. Because all previously described vaginal cysts said to originate from vaginal glands are also lined with simple epithelium.

The origin of the glands of the vagina is attributed to a displacement of cervical epithelium into the vaginal area of the ducts of Müller, or to a heteroplasia of the vaginal epithelium, practically constituting an erosion. This is believed for two reasons: 1. The cysts correspond to the ovula Nabothi. 2. The glands are exactly like the glands of the cervix. This view is upheld, although the cysts were arranged in a row like pearls and were situated in the lateral wall of the vagina.

Others who have found vaginal cysts lined with both cylindrical and squamous epithelium attribute their origin to the duct of Gartner and explain the presence of squamous epithelium through the opening of the glands of the duct of Gartner into the vagina. As will be seen later, squamous epithelium may result from the duct of Gartner.

Chalot believes that cysts should be attributed to the duct of Gartner if the epithelium is cylindrical or ciliated, if they are situated in the antero-lateral portion of the fornix and upper vagina, and if the cyst is continued into the paracervical or cervico-ligamentous areas. If not so continued, and if lined with papillæ, he believes such cysts to originate from cells of the ducts of Müller.

v. Recklinghausen considers that the absence of cilia, and a situation in the lateral walls of the vagina, speak for an origin from the ducts of Gartner. Cilia argue for an origin from the Wolffian body cells.

Amann believes that cysts lined with cylindrical or ciliated epithelium, either single or arranged in pearl form, and extending into the upper part of the vagina or into the broad ligament, are due to the ducts of Gartner.

(α) Cysts in the Lateral Wall.

In a tabulation of fourteen cases, six were ascribed by their authors to the duct of Gartner. Veit attributed to the duct of Gartner a case of vaginal cysts arranged in pearl form which were combined with a cystic tumor in the parametrium originating from the duct of Gartner, yet squamous epithelium was found in the cysts.

Kleinwächter found an adenoma in the upper part of the vagina, attached by a broad base, and containing cysts like those originating from the parovarium. He attributes their origin to the Wolffian body or to the Wolffian duct.

(β) Cysts in the Posterior Wall.

In a tabulation of nine cases not one was referred to the duct of Gartner. Most were referred to vaginal glands, depressions of vaginal mucosa, or to a rudimentary vagina. They were usually lined with cylindrical epithelium. Squamous epithelium was often present, and cilia

were also found. If the origin of these cysts is not to be attributed to the Wolffian body, it is difficult to explain the position and the presence of cilia except on the theory of Ruge. Nagel and Kossmann say that the vagina develops from the solid end of the ducts of Müller and is always squamous. Klein says it develops from the tubular distal end of the ducts of Müller and is at first lined with cylindrical epithelium. Ruge found ciliated epithelium in addition to squamous in hematocolpos, and holds the view mentioned by Klein.

(γ) Cysts in the Anterior Vaginal Wall.

These are found to be lined with cylindrical, squamous, or ciliated epithelium. In a tabulation of twenty-six cases, ten were attributed to the ducts of Gartner. Others were attributed to Littré's glands, vaginal glands, vaginal mucosa, and rudimentary vagina.

(Δ) Cysts Scattered Over More than One Wall.

Of six cases three were attributed to the duct of Gartner. These three extended from below upward, being more anterior below, and passing then more posteriorly up to the fornix. Cylindrical epithelium was present in all; in one case squamous epithelium was found.

Considerable light is thrown upon this question by Vassmer. He found a vaginal cyst in the lateral fornix of a 14-year-old girl which certainly originated from the duct of Gartner. It began one-half centimetre from the fundus uteri, consisting of three round lumina situated in the parametrium and surrounded by a connective-tissue mantle. On approaching the uterus they united into a common canal, entering the myometrium with the loss of the connective-tissue mantle, and passing internally and posteriorly into the cervix where it was situated near the lumen. In the vaginal portion it was found more external, ending near the fornix in the middle of the cervical wall. In the fornix the lumen was small, becoming gradually wider, and finally developing into a cyst with branching glands.

On the vaginal wall were papillary prominences situated posteriorly and laterally. Into some of these prominences passed several glandular branches from the cyst. Further down in the vagina no traces of the duct were found, but papillary prominences were present on the lateral and anterior vaginal walls.

From the parametrium into the cervix the lining of the ducts was simple epithelium. In the vagina this epithelium was also present, but it was not so high as in the cervix. The cyst was lined with epithelium in one and two layers. Crypt-like branches were present. The cyst contained islands of stratified squamous epithelium. In certain portions a gradual transition from cylindrical to squamous epithelium was evident.

In the parametrium the duct of Gartner possessed a tunica com-

posed of a layer of circular and an external layer of longitudinal muscle fibres. In the myometrium it was surrounded by connective tissue only. In the cervix the connective-tissue covering was lost, and here the glandular branches lay free in the muscle of the vaginal portion, as was also the case in the vagina, where the cysts possessed no muscle wall, but lay free in the connective tissue under the vaginal mucosa. A duct of Gartner was also found on the other side. It may be seen that squamous epithelium may be present in cysts of the duct of Gartner, and it is quite possible that the communications found between cysts and the vagina are simply the openings resulting from the growth of such cysts toward the vagina. Even though cilia have not been found in the duct of Gärtner, it is quite possible that such may be present. In addition, cells of the Wolffian body may be the cause. It is also probable that the arrangement of cysts in a pearl-like row indicates an origin from the duct of Gartner, for such have been followed up into the paracervical tissue.

The points which speak in favor of an origin from the duct of Gartner are: 1. A situation in the fornix and upper third of the vagina on the lateral or antero-lateral wall. The nearer to the vulva the cysts approach, the nearer are they situated to the mucosa and the more they approach the middle of the anterior wall. 2. An epithelial lining of cylindrical epithelium, or of both cylindrical and squamous. Cilia are possible. 3. The occurrence of papillæ, which are rare. 4. An arrangement in pearl-like form. 5. Extension into the fornix and further up. The walls of these cysts are usually composed of the connective tissue belonging to the duct of Gartner, and sometimes contain muscle fibres. The presence of the latter, while not necessary for making a diagnosis, is nevertheless a point of importance.

CYSTS OF THE LABIUM MINUS.

(A) Normal Anatomy.

Glands of the Vulva in the Fetus and Newly-Born (Robert Meyer).

The epithelium of the vestibule is of entodermal origin, and in the fetus up to five months is quite different from ectoderm. It extends often to the base of the nymphæ, anteriorly on the area leading to the frenulum clitoridis, posteriorly to the frenulum pudendi, and even to the commissure of the labia majora. This vestibular epithelium is displaced in the later fetal months by ectoderm, and islands may be left behind of stratified cubical and transitional cells. This epithelium lines especially the glandular depressions in the sulcus vestibuli.

Glands of the Vestibulum.

These are rarely entirely around the vaginal opening. The roof of the vestibule evidences mucous glands normally only in the preurethral area. They are absent behind the urethra. Mucous glands are sometimes present in the paraurethral section of the sulcus vestibuli, usually only glandular depressions. Behind the duct of Bartholini is a rudimentary double extension of the same. Physiologically only one such accessory duct is present; sometimes one or more additional have been found. Often glandular depressions with stratified cubical epithelium are found in the sulcus nympho-hymenalis.

Glands in the Fossa Navicularis.

These are: 1. Long gland tubules extending upward and retro-vaginal, in the muscle of the vagina or in the recto-vaginal septum. 2. Mucous cysts. 3. Islands of transitional epithelium.

Glands of the Hymen.

These are: 1. Vaginal glands on the inner vaginal surface. 2. Rests of the Wolffian duct. 3. Tubules from the fossa navicularis. 4. Genuine glands of the external vestibular layer. 5. Depressions of the latter. 6. Cysts with squamous epithelium, also derived from the epithelium of the external layer (rare).

Glands in the Nymphæ.

These are: 1. Glandular depressions derived from the sulcus vestibuli. 2. An heteropia of the vestibular epithelium. 3. Beginning sebaceous glands (?). 4. Squamous epithelium cysts. 5. Sebaceous cysts in the sulcus interlabialis. 6. Mucous cysts in the inner surface anteriorly near the frenulum clitoridis.

All mucous glands of the vulva and all the long extensions in the nymphæ and posteriorly to the perineum are referred to the entodermal epithelium of the vestibule. The ento-ectodermal boundary disappears in late fetal life and the glandular depressions disappear. The mucous glands of the preurethral area and of the accessory duct of Bartholini, the mucous glands and solid extensions with transitional epithelium, may remain under the ectoderm. In the clitoris a pair of glands is often present. Their origin is not known (Robert Meyer).

(B) PATHOLOGICAL ANATOMY.

The cysts are of three kinds:

1. From the normal elements of the labia minora, and therefore

either sebaceous retention cysts or atheromata with contents of a sebaceous character with concrements and cholesterin. Another form is lymph cysts.

2. From structures pathologically present: *(a)* displaced cells of cysts, *(b)* abnormally formed glands from the labial epithelium. The labium minus is ectoderm and no mucous glands can develop from this epithelium, nor are there any in it generally. Between the urethra and the introitus vaginæ are the glandulæ vestibulares minores. Between the hymen and the small labia are the glandulæ vestibulares majores (Bartholini). From displaced cells of these glands or from the glands themselves are formed cysts which may be of an acinous character, occasionally containing cilia, and also cystoid growths. *(c)* Retained entodermal cells.

(3) Cysts from the Duct of Gartner.

It ends at the sides of the introitus vaginæ or in the hymen in the external epithelial layer. An ending in the labia minora has not yet been found. Such cysts may be lined with cylindrical epithelium and papillæ. Another form is found in the upper third of the labium, including the vestibule, between the clitoris and urethra. These are lined with cylindrical epithelium, simple and stratified, also showing cilia and not infrequently squamous epithelium. The third form is glandular cystoma.

Weber attributes the origin of such cysts to the duct of Gartner for the following reasons: 1. If the Wolffian duct persisted it would remain in the upper part of the urogenital sinus and therefore in the upper third of the small labia. 2. These cysts are deeply situated, in contradistinction to the superficial retention cysts. 3. The diagnosis is assured if there is a continuation along the vagina up to the fornix. 4. The wall consists of connective tissue and often muscle fibres. 5. These cysts make a very early appearance and their growth is painless.

IV. TUMORS RESULTING FROM CELLS DISPLACED BY THE WOLFFIAN BODY AND WOLFFIAN DUCT.

(A) Normal Anatomy.

The primary vertebræ are embryonal masses of mesoderm lying on each side of the chorda and medullary canal. In the human embryo their number, extending along the length of the body, is 35 to 37. They are bounded externally by ectoderm, mesially by the medullary canal, and ventrally by the aorta. Between the primary vertebræ and the divided but unsegmented mesoderm there develops in the body segment the "intermediary band."

Fig. 100 shows the dorsal portion of the body mesoderm changed or segmented into "primary vertebræ." The ventral portion of the mesoderm is not segmented, but is divided so that the celom results. The mesial wall of each primary vertebra opens and the cells filling its centre, the nucleus, pass out of the primary vertebræ. These cells form the sclerotom. The cells which have passed out envelop the medullary canal and the chorda and form the cartilaginous and subsequently the bony vertebræ. The form of each primary vertebra then gradually changes and becomes long and four-sided. It consists of a mesial plate (the muscle plate), a lateral plate (the cutis plate), and an upper and a lower angle. This is the myotom, from which originate the segmented striated muscles of the skeleton. The primary vertebræ furnish, through the myotom, striated muscle fibres and a portion of the mesenchym.

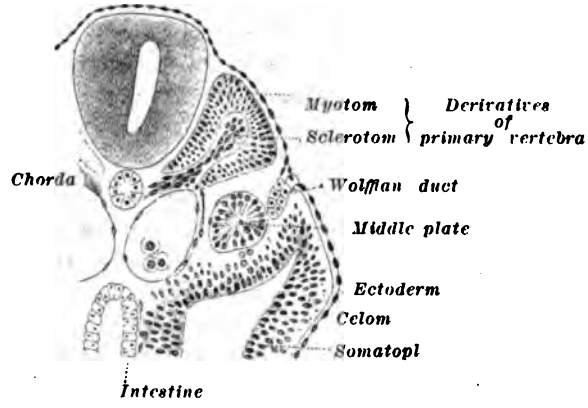


FIGURE 100.—SECTION THROUGH A "PRIMARY SEGMENT" AT THE POSTERIOR END OF A THREE-WEEKS-OLD EMBRYO. *(Hertwig.)*

Mesenchym tissue is that part of the mesoderm which spreads everywhere as the interstitial substance between the epithelial elements of the body, and forms smooth muscle fibre, mucous tissue, fibrous connective tissue, cartilage, bone, the lymphoid organs, blood vessels (?), blood (?), etc.

The visceral layer of the divided mesoderm, which includes the celom, becomes the mesoderm of the intestinal canal. In addition to forming the connective tissue of the lungs, of the liver, and of the pancreas, it forms the submucosa of the intestine and the muscle fibres of the intestinal wall. It furnishes also the mesodermal elements of the mesentery and the omentum.

The parietal layer of the mesoderm becomes the mesoderm of the body wall and is connected externally with the ectoderm. It is invaded and filled out later by the ventral angle of the myotom growing forward toward the anterior median body line.

On the dorsal wall of the celom, where parietal and visceral mesoderm unite, lies a cell called the intermediary band and "middle plate." Here the Wolffian body develops.

Most authorities say that the "middle plate" is a derivative of the primary vertebræ and forms the Wolffian body. We hold that the Wolffian body develops in the mesoderm at this point, but that it is, at least partially, a product of the ectoderm, as is also the Wolffian duct. We hold further that, though situated on the celom epithelium, the germinal epithelium is of ectodermal origin, resulting from cells carried down by the Wolffian body. At any rate, it is highly probable, on the authority of Spee, that ectodermal cells take part in the formation of the ovary. The peritoneum results from the celom epithelium and is of mesodermal origin.

In Fig. 100 is seen the "middle plate" at which later the Wolffian body develops. The Wolffian duct is also present close to the ectoderm. It is to be noted that they are not very close to the myotom, from which striated muscle develops, but lie in the mesodermal tissue, in the mesenchym which furnishes smooth muscle fibres.

The Wolffian duct lies next to the ectoderm, which furnishes epidermis, hair, nails, the entire central nervous system, and the spinal ganglia. The Wolffian body and the Wolffian duct are able to carry with them in their changes of location ectodermal and mesodermal cells, which later produce those structures which they were destined to form had they remained in their normal situation.

(B) Pathological Anatomy.

(α) Mixed Tumors of the Kidney

To show the position of the Wolffian body it must be mentioned that an undescended testicle and the epididymis have been found united to the spleen in a premature fetus which showed numerous anomalies of development. The origin of this condition is to be referred to that period of embryonal development in which the anterior portion of the Wolffian body and the Wolffian duct (later the epididymis and the vas deferens) extend up to the region of the liver and are united to the diaphragm by the diaphragmatic band of the Wolffian body (page 178). Since the spleen develops in this region, a union between it and the cells of the subsequent testicle and epididymis must be taken for granted.

The kidney finally develops in the position previously occupied by a portion of the Wolffian body. Mixed tumors of the kidney, described as rhabdomyoma, chondrosarcoma, angiosarcoma, myxosarcoma, and sarcoma, generally occur in early years, mostly in children under three years of age. A case in the fetus has also been described. They are situated mostly in the pelvis of the kidney or in the kidney substance, growing into the kidney as something foreign. They may be also situated out-

side the kidney capsule, which speaks against their origin from the kidney tissue itself. The colon has also been found behind the tumor. In addition to glandular structures are found smooth and striated muscle fibres, cartilage, fat, elastic fibres, colloid and fibrous connective tissue.

Birch-Hirschfeld and others believed that these tumors originate through the medium of the Wolffian body. Wilms believes that they originate from mesodermal cells in the neighborhood of the Wolffian body which are displaced by the latter. He therefore calls them "mesodermal tumors."

According to Wilms, the tubular glands are not primary structures, but are outgrowths of certain cells of the embryonal tissue still in a stage of differentiation. From this embryonal tissue (the mesodermal cells in the region of the Wolffian body) originate all the above mentioned structures and also the glandular elements. The round cells of these tumors are not sarcoma cells; they are embryonal cells which in their early stage have round-cell forms, and later, when differentiated, form epithelium, glands, etc. (see Cytogenic Tissue). These cells must orginate from a common area, because cartilage and striated muscle fibres are not found in the Wolffian body, and the displacement of cells forming these tumors from the substance of the Wolffian body alone, without participation of mesodermal cells, would not explain the presence of these two tissues.

(*β*) Retroperitoneal Dermoid Cysts.

Dermoid cysts are found in the abdominal cavity, but are always retroperitoneal. Muus described a mixed tumor of the kidney in which he found horny pearls. These were surrounded by epidermis-like cells. The presence of a stratum mucosum granulosum with keratohyaline nuclei and a stratum corneum proves them to be epidermis. This is a proof that in the displacement of cells cell groups, including both ectodermal and mesodermal cells, may be carried along. This is a proof that such a displacement of cells is not always of regular character, but is one which occurs with all possible variations, at one time more, at another time fewer, cells being removed from their original situation.

Dermoid cysts in various situations of the abdomen have been described. Marchand mentioned a solid dermoid cyst directly behind the kidney. Meckel reported one, containing twenty-one pieces of bone, teeth, and hair, situated near the diaphragm. Bonfigli mentioned a dermoid cyst, 13 cm. long and 4 cm. wide, situated in a strand extending from the liver and stomach. Zweifel described a retroperitoneal dermoid cyst extending from the diaphragm into the pelvis, pushing the kidney before it. Bardenheuer reported a retroperitoneal dermoid which had pushed the ascending colon posteriorly and externally and which was covered by the transverse colon. The pancreas was closely united to

the tumor. Pommer describes a dermoid cyst situated in the omentum, and Mayer one attached to the mesentery of the colon on the right side. All these are to be brought into genetic relation with the ectodermal origin of the Wolffian duct.

In Figs. 80 and 82 we seen the Wolffian body situated in the tissue which furnishes the mesodermal elements of the mesentery and the other abdominal organs. This tissue also forms the omentum, and it is only a question of the original position of the dislocated cells which determines in what portion of the mesentery such tumors may develop.

(γ) Mixed Tumors and Dermoid Cysts of the Ovary.

Dermoid cysts of the ovary frequently contain, in addition to epidermis and hair, smooth muscle fibres, cartilage, bone, teeth, connective tissue, neuroglia cells, structures like spinal ganglia, and cysts. The latter may be lined with simple or stratified cylindrical epithelium or with ciliated epithelium. The inner surface may show papillary excrescences, or may be lined with crypts containing beaker cells. In other words, we find in these dermoid cysts the same glandular structures as are found in the various adenomata, cystomata, and cystadenomata of the ovary whose origin we have referred to the Wolffian body tubules.

Our embryological discussion has furnished us with the following points, to which are added previously mentioned pathological statements:

1. The pronephros furnishes, through its tubules, direct communication between the ectoderm and the celom.

2. The Wolffian body furnishes, through its tubules, communication between the celom and the Wolffian duct.

3. The Wolffian duct develops near the ectoderm and in all probability from the ectoderm.

4. The ovary develops from certain cells situated on the celom, the germinal epithelium. Cells from the Wolffian body mesoderm are concerned in the development of the ovary, and the tubules of the Wolffian body may themselves be employed in forming the ovary.

5. Although the tubules of the parovarium usually are considered as ending blindly at the hilus, they actually extend into the vascular layer of the ovary, and

6. The parovarian tubules may be found, as v. Franqué has shown, in all parts of the ovary, even under the surface.

7. The cystadenomata of the ovary develop from remnants or tubules of the Wolffian body.

8. The various parovarian formations of the broad ligament show ciliated epithelium and are the remains of multiple segmental unions between the Wolffian body and celom and the Wolffian duct.

9. The broad ligament represents the epithelial celom covering and the connective-tissue basis of the Wolffian body.

10. The isolation of groups of cells from their normal relation and their removal from control is to be considered the cause of neoplasms.

11. The cystadenomatous structures found in ovarian cysts are found also in dermoid cysts of the ovary.

12. Pseudomucinous cystadenoma is often combined with dermoid cysts in the same or other ovary.

13. The mixed tumors and dermoid cysts of the kidney and those situated retroperitoneally develop from mesodermal and ectodermal cells displaced by the Wolffian body.

Therefore the pronephros, the Wolffian body, and the Wolffian duct, through their position in the mesoderm, their connection between ectoderm and celom, their relation to the normal development of the ovary, their subsequent position at the hilus of the ovary, and the extension of the tubules into the vascular layer and their growth through the ovary even up to its surface, and from the fact that their remnants furnish the ciliated growths of the broad ligament and form the cystadenomata of the ovary, are capable of carrying with them mesodermal and ectodermal cells up to or into the ovary, and of forming mesodermal and ectodermal products and structures lined with ciliated epithelium.

Cysts of the testicle lined with ciliated epithelium originate from remnants of the Wolffian body tubules. Therefore the mesodermal tumors, the mixed tumors, and the dermoids of the ovary and testicle originate in this same manner. Cystadenomata of the testicle frequently include in their stroma cartilage centres or show other elements.

Almost all the tumors of the testicle included under the names cystoid, enchondroma, rhabdomyoma, cystosarcoma, and cystocarcinoma, together with mixed tumors of the testis, are found, on careful examination, to contain ectodermal products. It is evident that just as the mesodermal mixed tumors show the various mesodermal tissues in varying degrees, so may also the mixed tumors which are built of both ectoderm and mesoderm. If ectodermal cells are displaced to any extent, so that their presence is manifested by cutis-like tissue, hair, sebaceous glands, etc., we speak of dermoid cysts. If the displaced cells are, so to speak, located in one part of the organ concerned, and if they grow equally, and if the skin cells, as in the normal skin, and the sebaceous glands excrete their products, a cystic dermoid must result. Since the contents found in dermoid cysts are excreted by the so-called "derm" of the cyst, they must lie, when secreted, between the derm and the enveloping tissue composing the organ or tissue in which the dermoids grow. The larger the amount of this secretion, the greater is the pressure exerted on the surrounding tissue. If the mass of secreted matter reaches a fair amount, and if it causes a tissue growth in its periphery, and if it compresses the enveloping organ or tissue so that it is stretched and flattened, we then have a cystic dermoid whose wall consists of so-called "skin," of granulation tissue, and of the tissue of the enveloping organ. The original group of displaced cells is found then as a prominence only in one part of the so-called cyst wall, and it is this part which grows grad-

ually for years, and in which are formed the hair, the sebaceous glands, and the other elements found on the inner surface of a dermoid cyst. The greater the amount of substance secreted, and the greater the amount and the number of products formed by the displaced ectodermal and mesodermal cells, the larger is the cyst.

If, on the other hand, the displaced cells are not grouped in one part of the organ concerned, and if, at the same time, the ectoderm cells are not present in too great number, there develops a tumor in which the various tissue forms grow into each other. Since the ectoderm cells do not form in such a case a so-called "derm," and since they cannot bring about the formation of a cyst through their excretion, as above described, a tumor form results which is relatively solid and which seems to be of an entirely different structure—a so-called "teratoma."

We understand under teratomata only the tumors originating from displaced cells, and we may therefore divide the so-called "teratoid" growths into

1. Mixed tumors.
2. Dermoid cysts.
3. Teratomata (solid dermoid cysts, usually of complicated structure).

It is, of course, to be understood that all these forms are only mixed tumors. The so-called "mixed tumors of the ovary" are of the following forms: enchondroma and osteoma, which are rare; cystic sarcoma, myxofibroma, adenomyxocystoma. In comparison with the mixed tumors of the testicle they are rare. A comparison of the mixed tumors found in the ovary with those in the testicle shows that in the latter there is a prevalence of mesoderm products with a relatively infrequent presence of ectoderm elements. In the ovary, however, these tumors occur more frequently in the form of dermoid cysts than in the testicle. This may be explained by the fact that in the female the Wolffian duct and the Wolffian body lie at the hilus as non-functionating organs, while in the male they form the vas deferens and functionating tubules.

That enchondromata and osteomata occur frequently in the ovary seems to be overlooked, because these, almost without exception, occur in combination with ectoderm cells, *i.e.*, as dermoid cysts and solid dermoids. This difference is explained, as above, by the fact that the Wolffian body and duct in the female remain as regressive structures and are more liable to growth on their own part and on the part of the cells which they have displaced. On the other hand, the Wolffian duct in the male forms the vas deferens, and a portion of the Wolffian body forms the head of the epididymis and the rete testis, while only a part undergoes regressive changes, and this part has not, like the Wolffian duct, been in close contact with ectoderm.

In ovarian dermoids and teratomata ectoderm is present in large amount. Therefore teeth are frequently found, and their occurrence

is in contrast with their rarity in the testicle. The origin of teeth is to be explained by the united presence of ectoderm and mesoderm in these tumors. It is difficult to understand why, in the higher vertebrates, teeth normally occur only in the mouth, for those tissue combinations which are necessary for the building of teeth, and which occur in the oral cavity, are also present in other parts of the body. Kollmann says: "The early cell formation and development of teeth is explained by comparative anatomy as a continuation of the tooth formation present upon the surface of the body of the lower vertebrates. The skin teeth, an evident organ of protection, are continued on into the oral cavity. Upon the jaws they reach, with their higher function, a higher stage of development. Their development in epithelium with the aid of mesoderm is a primary occurrence. Even in the lowest animal forms the teeth develop only through the participation of both these tissues."

In dermoid cysts the teeth are embedded in bone, or in the wall of the cyst where no cartilage or bone is to be found; they may also lie in the cyst contents. Their number varies, even one hundred or more having been found in one cyst. The teeth lie, as a rule, on the inner surface of the cyst, and are rarely embedded completely within the wall—another fact which speaks for their origin, as explained above, for ectoderm or skin is found on the inner surface. A further interesting fact is that the teeth, in all cases which we have examined, are always unilateral and, with perhaps one exception among eleven cases which were examined for me by a skilled observer, correspond to that side of the body in which the cysts are found, *i.e.*, in right-sided cysts were found right-sided teeth; in life-sided cysts, teeth of the left side. The occurrence of teeth in dermoid cysts is not limited to the ovary alone, for they are found in dermoid tumors in the brain, the eye, the mediastinum, and in abdominal dermoids. The teeth may be either first or second teeth, and both forms may be found in the same tumor. They may be either molars, bicuspids, incisors, etc., and may represent the teeth of the upper or lower jaw.

The dermoid cysts of the ovary do not always take their origin from the ovary. If, however, they do, the ovary may be entirely dilated by the tumor which has developed in it. On the other hand, the ovary may be found only in one part of the cyst wall in cases where the dermoid cyst originated at the hilus and grew into the broad ligament. Dermoid cysts may develop in the broad ligament, and the ovary takes no part in the formation of the tumor, but lies absolutely free, showing, however, as a rule various changes.

Switalski found, in examining the ovary and appendages of a fetus, an ectodermal structure lying close to the Wolffian duct in the broad ligament near the hilus of the ovary. Cells of the stratum granulosum and stratum lucidum of the epidermis were present, as well as cells of the stratum corneum. Its close relation to the Wolffian duct makes the etiological connection between the dermoid structure and the Wolffian duct positive.

The cells from which dermoid cysts develop may be carried into various parts of the ovary, so that several dermoids are present. Olshausen found in one case a proliferating cystoma of the ovary with two dermoid cysts of the size of an egg. In another case he found three dermoid cysts side by side. Wilms reported a case where five small dermoid cysts were present in one ovary.

Among the other interesting structures found in dermoid cysts must be mentioned nails (finger nails), of which very fine specimens are to be found in the museum of the Anatomical Institute in Vienna. Olshausen says: "It should not be considered strange if nails belonging to the skin are frequently found in dermoid cysts. The collection in the Gynecological Clinic in Halle contains a specimen of a dermoid cyst of a goose containing a large number of feathers."

The dermoid cysts are frequently combined with proliferating cystomata. As a rule a cystoma is found in the same ovary in addition to a dermoid cyst, but more frequently there are found in the walls of the dermoid cysts smaller or larger formations of the same character as in simple proliferating cystomata. These two forms are to be distinguished from these combinations of two separate tumors, the one a dermoid, the other a cystoma, united through adhesion and perforation of the separating walls. The occurrence of a dermoid in one ovary with a cystoma in the other is by no means rare. Olshausen quotes a case of Flaischlen in which a proliferating cystoma, a dermoid cyst, and a sarcomatous degeneration of the connective tissue were present in the same ovary; the walls of the cyst showed sarcomatous degeneration. A case of Unverricht showed, in the left ovary, the characteristic elements of a dermoid, and also red, spongy masses which were included as distinct nodules in the connective-tissue capsule. The case presented a round-celled sarcoma. Tumors of the same form were found in the cervix, peritoneum, omentum, liver, and diaphragm. Although the tumors in these latter situations are to be considered metastases, that in the cervix probably originated from the Wolffian duct in the same way as the main tumor in the ovary. That dermoids and teratomata should form metastases and undergo malignant degeneration into carcinomata, etc., is very natural, for they are nothing else than the cells of the patient, and may, therefore, pass through the same changes as the normally situated cells of the body.

(*A*) Mixed Tumors of the Vagina and Cervix Uteri.

In Fig. 94 we see the ducts of Müller and the Wolffian duct, the ureters (*U*) and the future bladder into which they empty. The point *S* (Fig. 90) becomes the hymen, and it may be seen that the Wolffian ducts (*Wf. D.*) would reach to the vaginal outlet. If the Wolffian duct carries with it mesodermal and ectodermal cells, it may be seen that they would lie (1) parallel to the future uterus, cervix, and vagina, or (2) between the uterus or cervix and the bladder, or (3) between the vagina

and uterus on the one hand and intestine on the other, but always external to the peritoneum. (See Fig. 90, where *C* represents the fold of Douglas, and where *X* represents the vesico-uterine fold.)

Mixed tumors of the vagina (rhabdomyoma sarcomatodes, sarcoma fibrosum, myofibrosarcoma with striated muscle fibres, etc.) and mixed tumors of the cervix uteri (containing sarcomatous tissue with cartilage, striated muscle fibres, etc.) are attributed by Wilms to cell dislocation on the part of the Wolffian duct. This cell dislocation is not a displacement of finished cell elements, but is a removal of as yet undifferentiated mesoderm or mesenchym cells, which form only at their future seat of development tissues corresponding to the normal embryonal differentiation.

Sarcoma of the vagina in children occurs during the early years and is characterized by its grape-like form. It almost always originates from the anterior vaginal wall. It is further characterized by a tendency to grow into the connective tissue between the bladder and the vagina. In many of these cases striated muscle fibres are present.

In adults sarcoma of the vagina is either circumscribed or diffuse. It is never papillary as in children. It occurs as frequently on the posterior vaginal wall as on the anterior. In adults striated muscle fibres are infrequent.

The same explanation as to origin is given for mixed tumors of the bladder wall and of the vas deferens. These mesodermal cells produce, later on, cartilage and myxomatous tissue, etc.

According to Englisch, cysts of various forms, which are especially situated on the posterior wall of the bladder, and more especially between the bladder and rectum of the male, originate from remains of embryonal structures, from the Wolffian body and the ducts of Müller, or through cystic dilatation of the seminal vesicles and prostatic sinus.

(ε) Dermoid Cysts of the Cervix.

These are not common. Geyl described one containing among other tissues bone, muscle fibres, nerve, etc. Küster and Nélaton have described dermoid cysts between the bladder and the uterus, but properitoneal.

(ζ) Dermoid Cysts of the Pelvic Connective Tissue.

Dermoid cysts in the region of the bladder are rare. Martini reported a case where the posterior wall of the bladder had the character of the external skin and was furnished with hair and hair follicles (trichiasis vesicæ).

Many cases classified as dermoids of the pelvic connective tissue are vaginal dermoids, because they have originated in the paravaginal cell tissue. These may, considering the course of the duct of Gartner, be

reckoned with dermoid cysts of the paravaginal tissue, just as vaginal cysts originate from remains of the duct of Gartner.

Dermoid cysts of the pelvic connective tissue are situated in the subperitoneal connective tissue between the rectum and the coccyx or between the rectum and the sacrum, or in the connective tissue beneath the fold of Douglas and above the recto-vaginal septum. They are situated above the pelvic diaphragm. They occur more frequently on the left side. Some of these may originate through participation of the caudal intestine, and for that reason the epithelial cells which have been carried up (see page 173) may be situated more to the left, because of the situation of the rectum on the left side. Another portion of these are probably due to the Wolffian duct.

These dermoid cysts are distinguished from those of the ovary in several ways: 1. Situation, extent, structure, and growth are quite different from the intraligamentous subperitoneal cysts of the ovary, by which are meant also the proliferating cysts of the ovary and parovarium. 2. The situation within the pelvic connective tissue; the thin wall of these dermoids, which consists usually of one chamber; the characteristic displacement of the rectum, the vagina, the uterus, and the levator ani, and their growth downward toward the perineum, are typical. 3. A connection between dermoids of the pelvic connective tissue and the ovary has never been observed clinically or anatomically. 4. These dermoid cysts have a smooth, thin wall, containing little hair and rarely bone.

(η) Dermoid Cysts of the Uterus.

Dermoid cysts probably situated on the inner surface of the uterus have been described by Kiwisch, Wagner, Cousot, Bartlett, Stewart, and others. They have usually been described as pedunculated. As the majority of these have appeared during labor, after extraction by forceps, they have generally been classified as dermoids of the pelvic connective tissue which have been expressed through tears of the cervix, the vagina, or the perineum. It must be mentioned, however, that some of the descriptions ascribing their origin to the uterus are very positive.

We see that the Wolffian body and the Wolffian duct are in a position to take with them cell complexes into a fairly large area, as is observed in:

1. Mixed tumors of the kidney, in which are found smooth muscle fibres, striated muscle fibres, cartilage, fat, mucous tissue, etc.

2. Dermoid cysts of the kidney and retroperitoneal and mesenteric dermoids.

3. Mixed tumors of the cervix, vagina, bladder, and vas deferens, in which, among other elements, are found striated muscle and cartilage. As may be seen in Fig. 100, the Wolffian duct lies nearer than the Wolffian body to the myotom, from which come striated muscle fibres. The

further the Wolffian duct goes in its course to the cloaca, the further does its lower end become separated from the ectoderm; and since the lower end of the duct alone and not the Wolffian body is the origin of the mixed tumors and the dermoid cysts of the cervix and vagina, these occur in the latter situation less frequently than in the ovary. For this reason also the dermoids of the ovary rarely contain striated muscle fibres, because the Wolffian body and the upper portion of the Wolffian duct are not so near the myotom.

4. Dermoid cysts of the cervix and the vagina, and those between the bladder and the uterus and in the pelvic connective tissue.

5. Mixed tumors of the testicle, described under the names "adenocystoma, chondroadenoma, chondrosarcoma, adenomyosarcoma, etc.," in which are found cysts with cuboidal cylindrical epithelium, with or without cilia, as well as stratified ciliated epithelium, mucous tissue, cartilage, and sometimes muscle tissue, fat, and less frequently bone.

6. Dermoid cysts of the ovary and testicle.

That the mixed tumors of the cervix and vagina should have a less complex structure than the mixed tumors of the kidney is easily understood when we consider that the former are caused by displacement of cells by the Wolffian duct alone, for this does not come in contact with so many varying tissue cells of the mesoderm as does the Wolffian body, and when we consider, further, that its lower end, which finally reaches the future cervix and vagina, does not come in contact with the Wolffian body. For these reasons we rarely find in these latter mixed tumors of the cervix and vagina the numerous cystic formations which are present in growths resulting through the medium of the Wolffian body.

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